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CHOLECYSTOGRAPHY: ITS DEVELOPMENT AND APPLICATION*

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THE demonstration of the striking effectiveness of the roentgenological visualization of the alimentary canal by the opaque meal in the diagnosis of gastric and intestinal conditions, and of the kidney pelves after the intraureteral injections of opaque substances has led naturally to the desire to find some method by which other structures could be made to reveal to the eye their abnormalities. Because of the very great frequency of affections of the biliary tract it would be particularly desirable to have a method which would permit the visualization of the gall-bladder. Cholecystography has now for the first time been shown by us to be possible by a variety of substances. It has become a safe clinical procedure of unquestioned effectiveness in the diagnosis of abnormalities of the biliary tract, even in such mild cases of cholecystitis that an accurate diagnosis by any other means would be impossible. Its value lies not only in the ability to recognize gross pathological alterations of the biliary tract but also in the fact that it serves as a rather precise functional test of the gall-bladder. For this purpose the halogenated phenolphthaleins seem at present to be the most useful, and of these the sodium salt of tetraiodophenolphthalein has been found by us to be the most desirable up to the present time. Investigation of other substances is in progress, and it is possible that some more desirable compound may be found.

THEORY OF CHOLECYSTOGRAPHY

The theory upon which the procedure is based is that if any substance containing either a metal or atoms of bromine or iodine could reach the gall-bladder in sufficient concentration, then that organ would be made opaque to the roentgen ray. To be practical, the substance must be one which can be given either by the alimentary canal or by injection. Moreover it must be relatively non-toxic and sufficiently soluble to avoid the necessity of giving large volumes of fluid. In any case, presumably, it would have to be a substance which would be excreted by the liver and carried to the gall-bladder in the bile. Moreover, the ability of the gall-bladder to concentrate its contained bile, as shown by Rous and McMaster,[1] would indicate that a sufficient time must elapse before a shadow of maximal density would occur. Reasoning from these premises, the conclusion would have to be drawn that the shadows of sharpest contrast would be obtained in normal individuals. Similarly also no shadow would be expected to appear if the liver were unable to excrete the substance in sufficient amount, if the cystic duct were occluded,

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or if the function of the gall-bladder were sufficiently impaired to prevent the concentration of the material. Intermediate degrees of changes from the normal conditions will result in the appearance of shadows which will require for their interpretation a skill which can be obtained only by an extensive experience with the method. All of these conclusions have been found true as our own experience with the procedure has developed. These points will be discussed more elaborately in the section on interpretation.

HISTORY OF DEVELOPMENT

The work of Abel and Rowntree[2] in 1910 on the pharmacological actions of some of the phthaleins and their derivatives showed that many of these were excreted in large part in the bile, and it formed the basis of the extensive use to which some of them have been put as a means of determining the functional capacity of the liver. With this work as a starting point, it occurred to us that it might be possible to obtain roentgen-ray shadows of the gall-bladder if substances were used which would contain a nucleus identical with, or closely allied to, phenolphthalein with which iodine or bromine atoms had been combined. Experiments were begun in the summer of 1923. The first substance which we used was tetraiodophenolphthalein of the following formula:

Both the free acid and the sodium salt were used. By the use of this substance it was demonstrated in dogs that cholecystography is possible by the intravenous injection of a substance which contains a phenolphthalein nucleus. Unfortunately, however, it happened that our first preparation contained toxic impurities which resulted in the death of some of our animals. Thinking that the toxic results were due, in part at least, to inevitable decomposition products of the iodine compound we decided to try the tetrabromine product instead. By analogy with a well-known chemical fact that organic iodine compounds are usually less stable than the corresponding bromine compounds we concluded that tetrabromphenolphthalein would probably be less toxic than the tetraiodophenolphthalein. It was disappointing, however, to have to abandon temporarily the use of the latter because, theoretically, by virtue of the higher atomic weight of iodine, smaller doses of the tetraiodophenolphthalein should be required to produce good shadows. It was not until the summer of 1924 when we were able to procure some highly purified tetraiodophenolphthalein that we discovered that our former bad results were in large part evidently due to impurities which could be eliminated. This discovery permitted us to use the tetraiodo compound on the human subject with the gratifying result that relatively few toxic results occurred when doses were employed which were only about one-half as large as those necessary when the tetrabrom compound was given. In fact we are now using it fearlessly in outpatients who are permitted to go home after their injections. This finding, therefore, agreed with our theoretical premises. The results of the use of the tetraiodophenolphthalein have been incorporated in two recent articles.[3,4] More will be said about it below.*

For the reasons stated above, however, much of the early work, including the working out of the criteria of interpretation, has been done with the sodium salt of tetrabromphenolphthalein. The use of the tetraiodo compound does not change in any way the standards of interpretation as worked out for the tetrabrom. Presumably

* As stated, however, in our article of Jan. 3, 1925 (*J. Am. M. Ass.*), it is necessary to exercise more caution both in the manufacture and care of the tetraiodo than with the tetrabrom in order to avoid toxic effects. We were unwilling, therefore, to recommend the use of tetraiodophenolphthalein extensively until we felt sure that the manufacturers could insure a fairly standard product. This difficulty is now attracting attention in the literature. Whitaker and Milliken (*Surg., Gynec. & Obst.*, January, 1925, xl, 17) evidently were fortunate enough to secure a good sample of the product for use in their experiments and were unaware of the variability of products with the resulting danger from toxic effects. They are, however, entitled to the credit which belongs to any who make independent observations, and the report of their experiments has done much to popularize not only the use of cholecystography but of the tetraiodo itself.

the criteria of interpretation would be the same for any substance which would make the gall-bladder opaque to the roentgen ray. As will be seen below we have used many other substances experimentally. A vast number of possibilities exists; and it is therefore entirely possible that in the future some other substance will be found to be preferable to any of those which we have so far used.

The substances which we have used in the development of this work have for the most part been prepared for us by Dr. N. Drake of the Research Department of the Mallinckrodt Chemical Works, St. Louis. They are as follows:

I. Halogenated Derivatives of Phenolphthalein Compounds
   1. Tetraiodophenolphthalein
   2. Tetrabromphenolphthalein
   3. Octabromphenolphthalein
   4. Dibromphenolphthalein
   5. Diiodophenolphthalein
   6. Tetrachlorphenoltetrabromphthalein

II. Halogenated Derivatives of Phthalein Compounds
   1. Phenoltetrachlorphthalein
   2. Phenoltetrabromphthalein
   3. Phenoltetraiodophthalein

III. Sulphonated Halogenated Derivatives of Phenolphthalein
   1. Dibromphenolsulphonephthalein
   2. Diiodophenolsulphonephthalein
   3. Tetrabromphenolsulphonephthalein
   4. Phenoltetrabromsulphonepthalein (bromsulphalein).
   5. Tetraiodophenolsulphonephthalein

IV. Halogenated Derivatives of Resorcinolphthalein, or Fluorescein
   1. Fluorescein
   2. Tetrabromfluorescein (eosin)
   3. Tetraiodofluorescein (erythrosin)
   4. Tetrabromdichlorfluorescein (phloxin)
   5. Tetraiodotetrachlorfluorescein (rose bengal)
   6. Octaiodofluorescein
   7. Dibromoxymercurifluorescein (mercurochrome —220 soluble)

V. Miscellaneous
   1. Tetrabromphthalate
   2. Tribromphenol
   3. Hexamethylene-tetramine iodine compound
   4. Arsphenamine
   5. Carbamide tetrachloriodide
   6. Phenolphthalein
   7. Brilliant vital red
   8. Trypan blue
   9. Methylene blue
   10. Gentian violet
   11. Azorubin

Of this number, the salts of ten have been shown to have the power of making the gall-bladder visible, namely, tetraiodophenolphthalein, tetrabromphenolphthalein, octabromphenolphthalein, phenoltetrabromphthalein, phenoltetraiodophthalein, tetrachlorphenoltetrabromphthalein, tetrabromfluorescein (eosin), tetraiodotetrachlorfluorescein (rose bengal), tetraiodofluorescein and octaiodofluorescein. The last eight, however, have disadvantages which seem at present to preclude their clinical use, although it is possible that subsequent work will show that phenoltetraiodophthalein will prove superior to any of the others. Further work with this substance is now in progress.

PHARMACOLOGY

In their pharmacological reactions there is no appreciable difference between tetrabromphenolphthalein and tetraiodophenolphthalein. This is to be expected because of their similarity in structure. The clinical superiority of the latter lies in the fact that doses of only about half the size can be given with equally good roentgenological results. This practically eliminates the toxic effects which have been the chief obstacle to a more wide-spread use of the procedure. Tetrabromphenolphthalein has a molecular weight of 634, and it contains about 50.4 per cent of bromine. In contrast with this, tetraiodophenolphthalein has a molecular weight of 822 and it contains about 61 per cent of iodine. This difference of course is due to the fact that the atomic weight of iodine is 127, while that of bromine is 80; and it is because of this fact that equally good shadows can be obtained with much smaller doses of tetraiodophenolphthalein than with the tetrabrom compound.

The sodium salt of both the tetrabrom and the tetraiodophenolphthalein is a blue crystalline compound which is readily soluble in water. A 50 per cent solution can be obtained by heating. Prolonged exposure of even the dry salt to the air and light causes it to fade and increases its toxicity. It should therefore be kept in brown bottles.

Both substances have about the same degree of toxicity. With toxic doses they both produce the same general symptoms. Dogs readily tolerate well doses of 0.2 gram of either substance per kilo of body weight. We have not exceeded in the human, however, doses larger than 0.1 gram per kilo; and with the tetraiodo

compound satisfactory shadows are obtained with doses of 0.055 gram per kilo. Repeated examinations of small pieces of the liver from both the dog and the human after the administration of doses of this size have failed to reveal any abnormalities, although recently Ottenberg and Abramson[5] have shown that in doses of from four to six times larger than these, necrosis of the liver may be produced. No effect on the clotting time of the blood is observed with standard cholecystographic doses; but if these doses are exceeded, slight hemolysis may occur.

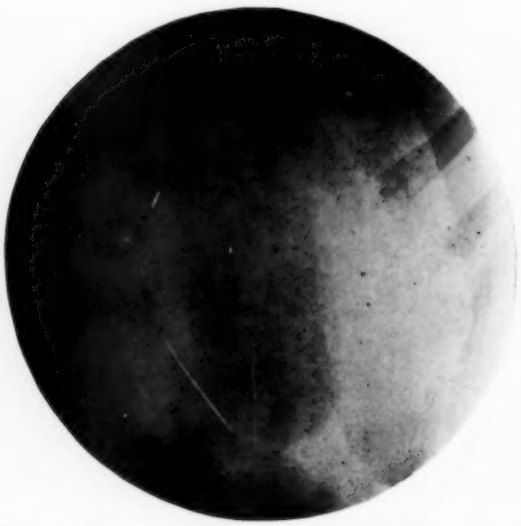

FIG. 1. A shadow of a normal gall-bladder appearing faintly eight hours after injection.

The color of the blood serum and of the bile is unchanged with these substances in contradistinction to the somewhat similar compounds, namely the phenoltetrabrom and the phenoltetraiodophenolphthalein. For that reason there is no satisfactory colorimetric method for their determination in either the blood serum or the bile. The substances fluoresce and have absorption bands in the spectrum.

Practically the entire bromine content of tetrabromphenolphthalein may be recovered in the bile after injection. A laparotomy was performed on a 6.4 kilo dog. The common duct was canalized with a small glass tube around the distal end of which was tied a rubber bag for the collection of bile. Another bag was likewise connected with the gall-bladder. The abdomen was closed and the dog was given 1 gm. of sodium tetrabromphenolphthalein intravenously. The animal was sacrificed at the end of forty-eight hours and 112 c.c. of bile collected from the two bags. The 112 c.c. of bile contained 0.4569 gm. of bromine. Theoretically one gram of the tetrabrom should contain 0.47 gm. of bromine. Thus, in this experiment 97 per cent of the bromine injected was recovered from the bile in a period of forty-eight hours. In two experiments to determine the amount put out in the bile in twenty-four hours after the injection of 1 gm. of tetrabromphenolphthalein, the results were 0.25 to 0.34 gm. of bromine respectively, or 53 per cent and 72 per cent respectively.

To 4 dogs sodium tetrabromphenolphthalein was given in doses of different amounts, and after twenty-four hours they were killed. Roentgen-ray films showed in each case dense gall-bladder shadows. The bile was collected from each of the gall-bladders and a quantitative analysis for bromine gave the following results:*

Dog	Weight, Kilos	Dose, Grams	C.c. of Bile	Grams of Bromine	Percentage Concentration of Bromine in Bile
238	10.0	2.0	11	0.0696	0.63
239	7	1.5	16	0.072	0.45
240	6	1.5	6	0.0504	0.83
241	8.4	2.0	19	0.1424	0.75

Excellent shadows therefore may be obtained by concentrations of bromine in the bile varying from 0.45 to 0.83 per cent. Certain unexpected difficulties were encountered in making the analyses for iodine in the bile after the injection of tetraiodophenolphthalein. For that reason it is impossible to state in this paper what concentration of iodine in the bile is necessary for the production of good shadows, but the presumption seems reasonable that a much smaller concentration of iodine will be required because of its greater atomic weight.

* These analyses were made for us by Mr. Shrewsbury under the direction of Professor P. A. Shaffer of the Department of Biological Chemistry.

Injections of both the tetrabrom and the tetraiodophenolphthalein are followed by a perceptibly increased flow of bile. These substances are not efficient biliary antiseptics in the concentrations employed for cholecystography, as evidenced by their effects on cultures of various bacteria.

Fairly rapid intravenous injections of the sodium salt of either substance induces a sharp transient fall of blood pressure of about 15 mm. of mercury in the dog. A prolonged injection over a period of ten minutes or longer may not be followed by a fall of blood pressure. We have never seen a rise of blood pressure to a point above normal after single or multiple injections either experimentally or clinically. A fall of blood pressure similar to that obtained after injection of the sodium salt of either substance can be obtained by the intravenous administration of an equal amount of phenolphthalein. Clinical cases have had careful blood pressure readings made at frequent intervals for a considerable time after injection, and in the majority of cases there have been no changes in blood pressure. In a few there has been a sharp fall. The marked falls of blood pressure were accompanied by systemic reactions. We have found that in those cases in which there have been falls in blood pressure accompanied by other symptoms prompt relief may be afforded in most instances by the administration of 0.5 c.c. of a 1 to 1000 solution of adrenalin chloride, as first suggested to us by Case.

Both substances are non-irritating when applied to the skin. In any considerable concentration, however, they will produce necrosis when injected into the subcutaneous or muscular tissue. Suspensions of the free acid and of the sodium salt in olive oil and a solution of the sodium salt in olive oil have been injected subcutaneously and intramuscularly into experimental animals. The gall-bladders of rabbits have been visualized by the roentgen ray in several instances with each of the preceding methods; but the shadows have been obtained inconsistently. No gall-bladder shadows have been obtained in dogs by either method. Usually the subcutaneous injection was absorbed in forty-eight hours without marked local reaction.

FIG. 2. The same gall-bladder after twenty-four hours. The shadow has become much more distinct and smaller.

FIG. 3. Thirty-two hours after injection. The shadow has become still smaller and less distinct.

Shadows of the gall-bladder may also be obtained after the administration of the substances by mouth. This method is being investigated at present. It would seem probable, however, that an intravenous injection must necessarily present advantages over the oral administration because, in the interpretation of the cholecystograms, it is necessary to know how much of the substance has

reached the liver. The uncertainty of intestinal absorption is present with any substance which is administered by mouth, and this uncertainty must be increased when the particular substance has a slightly laxative action, as is the case with the phenolphthaleins.

Of the other substances listed as having been tried, eight produced roentgen-ray shadows of the gall-bladder when injected intravenously, but all of the eight had certain disadvantages as compared with either the tetrabrom or the tetraiodophenolphthalein. The disadvantages consisted chiefly either of a toxicity too great to permit clinical use or of a general staining of the body tissue. Those substances which we have found to be capable of producing shadows of the gall-bladder have been mentioned above.

It was hoped that some of the sulphonated compounds which we studied might give rise to shadows of the kidney even if they did not produce cholecystograms, because, by the addition of a sulphone radicle, there is a greater tendency for many organic substances to be excreted through the kidney, as was shown by Abel and Rowntree in the case of the phenolsulphonephthaleins. Unfortunately, however, no kidney shadows were produced.

TECHNIQUE

In using either the tetraiodo or the tetrabromphenolphthalein it is essential that digestion should not be in progress at the time of injection. Otherwise no shadow may be produced even in a person with a normal gall-bladder. In order to obtain a shadow of maximal intensity it is necessary to have maximal secretion into the bile and maximal concentration of the substance within the gall-bladder. If food is present in the duodenum, our own and accumulated evidence seems to indicate that sufficient bile is poured into the intestine to prevent the maximal entrance or concentration of the dye in the gall-bladder. Accordingly the routine procedure which we now carry out for clinical use is as follows:

In the case of tetraiodophenolphthalein, 3.5 gm. of the sodium salt is dissolved in 28 or 30 c.c. of freshly distilled water for an individual weighing 125 pounds or more. The solution is filtered through a fine filter paper and sterilized in a boiling water bath for fifteen minutes. For convenience we have put individual doses into ampules and sealed them before sterilization. Solutions in ampules have been used without any change in toxicity for as long as three weeks after preparation. We do not know how long they may be safely kept before use. The solution is given intravenously in two doses, one-half hour apart, in the morning before breakfast, between 7:30 and 9 A.M. Care should be taken not to allow extravasation outside the vein during the injection. Solutions of tetraiodophenolphthalein made in this dilution may produce induration, but in our experience no sloughing of tissue has ever occurred. If the sodium salt of tetrabromphenolphthalein is used, a dose of 4.5 to 5 grams is dissolved in from 35 to 40 c.c. of freshly distilled water and injected as described above.

Certain orders for the patient are essential:

1. Breakfast should be omitted.
2. Lunch should be omitted, but the patient may have a glass of milk.
3. Protein should be omitted from the evening meal.
4. Water is allowed *ad libitum*.
5. Alkalinization of the stomach contents by frequent doses of sodium bicarbonate by mouth is helpful.

The rationale of the latter procedure is explained in a recent article by Cole,[6] who found experimentally on dogs that the flow of bile into the intestine through relaxation of the sphincter of Oddi is prevented or much diminished by keeping the contents of the stomach alkaline. This probably tends to promote the concentration of bile in the gall-bladder.

Roentgenograms are taken in series, at four, eight, twenty-four and thirty-two hours after injection. The following technique is used in making the cholecystograms. a radiator Coolidge tube is used with duplitized films under double intensifying screens. The smallest practical diaphragm is used, and compression is made with the cone on the patient, who

lies on his abdomen on the table. A flash exposure is made, a 60 ma. current with a 5-inch spark gap being used. The spark gap varies with the thickness of the patient. The Bucky-Potter diaphragm may be used, but it does not seem essential.

INTERPRETATION

If the technique described above has been carried out, a normal gall-bladder will show the following reactions: Usually at about the fourth to the seventh hour after the injection a faint but definite outline of the gall-bladder appears which is seen to have the contour of the normally shaped organ but to be somewhat larger than normal gall-bladders usually seen at laparotomy. At the end of twenty-four hours the shadow is much more distinct but contracted down to only about one-half of its earlier size. From then on until about the forty-eighth hour the shadow diminishes in size and fades gradually.

Abnormalities reveal themselves in various ways. A failure to obtain any shadow after carefully following the recommended technique has invariably indicated definite pathology of the biliary tract. It is conceivable, however, that in rare instances of very serious disturbance of hepatic function an insufficient amount of the substance might be secreted to produce a shadow even without any appreciable alteration of the gall-bladder, but we have not yet encountered this difficulty. Abnormalities of less degree have shown themselves by such phenomena as late appearance of a shadow, faintness of shadow, failure to diminish in size, distortion of outline, irregular mottling, etc. As experience with the method increases it becomes more and more evident that it is an index of function of the gall-bladder rather than one which shows sharply distinct pathological lesions. For example, two such different pathological conditions as obstruction of the cystic duct and a fibrosed gall-bladder without obstruction of the cystic duct will both usually result in a failure to obtain a shadow. The reason for this lies in the fact that, although in the first instance the substance has not been able to enter the gall-bladder, in the second instance the gall-bladder has not been able to exercise its normal function of concentrating the bile. In earlier work[7] one of us has called attention to the fact that cholecystitis is practically invariably an interstitial inflammation rather than one limited to the mucosa and that this is due very largely to the frequency with which cholecystitis has its origin in a lymphangitis secondary to a hepatitis. As a result of the obliteration of lymphatic vessels in the wall of the gall-bladder by inflammation, the normal ability to concentrate the bile which was demonstrated by Rous and McMaster[1] becomes seriously impaired. The sensitiveness of cholecystography in revealing abnormalities of function of the gall-bladder is one of its most striking assets in the diagnosis of slight degrees of cholecystitis. As our interpretation of cholecystograms has become more nearly perfected we have become more and more impressed with the fact that it is a more accurate method of revealing lesions of the gall-bladder than any other in our possession except that of adequate inspection and palpation at operation with generous exposure. In fact, in several instances we have removed doubtfully normal gall-bladders on the strength of the cholecystographic findings and later have found them to show definite signs of inflammation with the microscope. It is because of its sensitiveness to slight functional changes that cholecystography becomes of great value in the diagnosis of the cases of early and comparatively slight cholecystitis which are most difficult to diagnose by any other method, either clinical or laboratory. Heretofore most cases could be accurately diagnosed only after they had gone to the stage of advanced pathology with scarring, formation of stones, etc. In the sense, therefore, that this method presents the possibility of early accurate diagnosis it adds also the possibility of creating another chapter in preventive medicine. By early operative treatment, most of the ravages of long standing cholecystitis with its accompanying serious effects on the liver and pancreas can be prevented.

Gallstones have sometimes been visualized by appearing as "negative shadows" in the cholecystograms. That is, the places occupied by stones appear as areas of less density, doubtless because each stone takes the place of its corresponding volume of dye. More often, however, we have failed to visualize stones which were later proven at operation to be present, because usually a cholecystitis which is severe enough to be accompanied by stones fails to respond by any shadow of the gall-bladder at all. But the method has often proved useful in distinguishing between renal stones and gallstones. Adhesions have sometimes been recognized by distortions in the outline. Surprising abnormalities of position of the gall-bladder have been recognized; in one case, for example, a gall-bladder was found to be in the pelvis.

RESULTS

We have studied 261* individuals by cholecystography, using the intravenous injection of the sodium salt of either tetrabromphenolphthalein or tetraiodophenolphthalein. Of this number it has been possible to verify our roentgenological diagnosis in 80 patients upon whom operations have been performed. In this series our cholecystographic diagnosis has been found correct in 96.25 per cent of cases. In all the cases of operation on the gall-bladder the organ has been removed and subjected to microscopic examination. In the last 20 cases which have come to operation the cholecystographic diagnosis has been confirmed in every one. These diagnoses have been made for the most part by the members of the department of roentgenology. As in all other diagnostic methods, satisfactory skill in the interpretation of results will be acquired only by an extensive experience.

TOXIC ACTIONS

The chief deterrent to a more general use of the method of cholecystography in the past has been the toxic reactions which some patients have manifested. These have varied from slight dizziness and nausea in some cases to a condition of temporary collapse with a sharp fall of blood pressure in others. By using the sodium salt of tetraiodophenolphthalein in the dosage recommended above, however, these reactions have been practically eliminated and we are now using the method freely on outpatients, who are allowed to go to their homes after the injections. It would be advisable, however, not to inject any elderly patients, with low blood pressures or with bad cardiac conditions. Table 1 presents a comparison of the effects of sodium tetrabromphenolphthalein and sodium tetraiodophenolphthalein in a series of 21 patients each.

TABLE 1

A COMPARISON OF TWO SERIES OF 21 CASES EACH INJECTED RESPECTIVELY WITH SODIUM TETRABROMPHENOLPHTHALEIN AND SODIUM TETRAIODOPHENOLPHTHALEIN

	Sodium Tetrabromphenolphthalein		Sodium Tetraiodophenolphthalein	
	No. of Cases	Per Cent	No. of Cases	Per Cent
No reaction....	13	62	18	86
First degree reactions.....	4	19	3	14
Second degree reactions.....	1	4	0	0
Third degree reactions.....	3	14	0	0

Table 1 shows an absence of second and third degree reactions after injection of sodium tetraiodophenolphthalein. We have listed under first degree reactions those patients who suffered either a slight headache, vertigo or nausea lasting from a few seconds to ten minutes. Under second degree reactions we include those patients who sustained first degree reactions of slightly increased severity for a period of three or four hours. Third degree reactions include those patients who had nausea, vomiting, backache, slight tachycardia and temporary fall of blood pressure. Invariably the blood pressure in these cases soon returned to normal. Even the patients suffering the most severe reactions showed no evidence or symptoms of it the next day.

* At the time of going to press the number of patients subjected to cholecystographic examination was 540, using either the intravenous or oral route. The accuracy of the intravenous method has remained about 95 per cent. The accuracy of the oral method has been only about 80 per cent.

SUMMARY

1. Cholecystography, a new principle in the diagnosis of lesions of the biliary tract, has been introduced, consisting of the use of substances which after entering the blood stream are largely excreted in the bile and render the gall-bladder opaque to the roentgen ray.

2. At present the most satisfactory substance for clinical use is the sodium salt of tetraiodophenolphthalein. The technique of its use is described. There are many other substances which are capable of rendering the gall-bladder opaque.

3. This principle may be capable of application to the roentgenologic visualization of other organs, if opaque substances which are specifically secreted by such organs can be found.

4. The method of cholecystography owes its chief value as a diagnostic agent to the fact that it is a sensitive test of the function of the gall-bladder.

5. As a method of diagnosis it has been found correct in 96.25 per cent of 80 patients upon whom it has been possible to test the diagnosis by means of an operation.

6. The unpleasant toxic effects have been practically eliminated.

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CLINICAL AND EXPERIMENTAL CHOLECYSTOGRAPHY*

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CHOLECYSTOGRAPHY is now a routine diagnostic procedure in many clinics. The name of this test, the technique of performing it and all the diagnostic criteria have been thoroughly described by its originator, Dr. Evarts Graham, of Washington University.[1,2,3,4] There are several variations now in use, not only in the preferential drug,[5,6] but also in the method of administration.[7,8,9] We employ only two methods, the intravenous and the oral, using the sodium salt of tetraiodophenolphthalein in both.

The intravenous dose of the salt is 0.04 gm. per kilogram of body weight given in a single injection as a 2 per cent solution at body temperature. Smaller doses will produce shadows, but of less density. The injection is given late at night and the first films are made the following morning, usually at ten hours.

The oral dose is given as "enteric coated" pills, using one 5-grain pill for each 10 to 12 pounds of body weight. These pills are taken four at a time at half-hour intervals after the evening meal, and the first films are made the following morning at fifteen hours, with the patient fasting.

If by either method there are secured smooth, homogeneous shadows, of good density (as compared with a normal established by experience), then fat-containing food is given to the patient and an hour

* From the Department of Roentgenology, Peter Bent Brigham Hospital, and the Laboratory for Surgical Research, Harvard Medical School; read at the Twenty-sixth Annual Meeting, American Roentgen Ray Society, Washington, D. C., Sept. 22–25 1925.

later more films are made. If, at that time, the shadow has decreased definitely in size, a report of "normal gall-bladder" can safely be made. If, on the first plates, persistent negative shadows are seen, the examination is concluded and "gallstones" are reported. If, however, on the first films no shadow is seen or a shadow fainter than normal is recorded, more films are made at intervals (the patient still fasting) to see if the shadow subsequently appears or increases in density, as the case may be.

We have used the intravenous method in 120 patients. *Normal* shadows and function were reported in 54, of which 5 were explored surgically, with confirmation of our report in all but one. In 22 patients, *stones* were seen, appearing on the films either as large "negative" shadows within the opaque gall-bladder area, or as a fine even mottling of the shadow. In all the patients of this group operated upon, 17 in number, our findings were confirmed. Persistently *faint* shadows were found in 18 cases, causing us to report "pathological gall-bladders," "cholecystitis without stones," or "poorly functioning gall-bladders." Of this group 7 were operated upon, our impression being correct in five. *No shadows* were secured in 26 cases, of which 14 were explored, definitely pathological gall-bladders being found in all, and stones in 10 of them. In summary, the intravenous method gave us accurate results in 93.5 per cent of the cases.

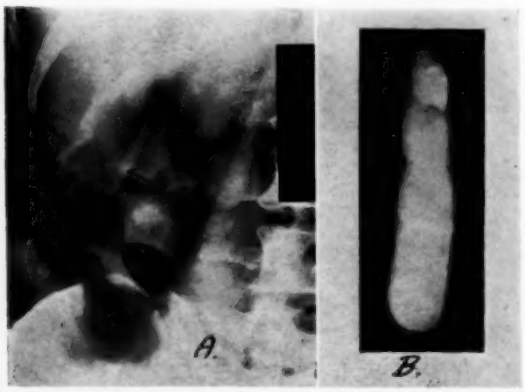

FIG. 1A. Intravenous method. A faintly outlined shadow with multiple large calculi, indicating both cholelithiasis and cholecystitis. Both confirmed.
FIG. 1B. Roentgenogram of excised gall-bladder.

The oral method has been employed in 243 cases to date (Sept. 1). Normal shadows and function were discovered in 132, stones were found in 20 cases, faint or absent shadows in 79, and in 12 the examination was unsatisfactory, due to mistakes by the patients in following directions, to wrong preparation of the pills, or to faulty technique. Operations in this second group totalled 21, the findings confirming our impressions in 20 and varying from them in one. Thus, in this group, 95.2 per cent of the cases explored surgically had received a correct diagnosis by oral cholecystography. The purely clinical preoperative diagnosis in both the intravenous and oral groups (as demonstrated at operation in 59 patients) was correct in 79.7 per cent of the cases.

FIG. 2. Oral method. A very faint, diffusely mottled shadow, indicating multiple small calculi, confirmed by intravenous method and by operation.

As a further check on the oral method, 39 of the patients who had by it presented signs indicating pathology were subsequently given the intravenous test, this confirming the first examination in 27 and disclosing normal shadows and function in the other 12, an accuracy of only 70 per cent.

A critical comparison of the two methods upon the basis of only 59 proved cases is hardly fair, but it is evident that the intravenous method is much more reliable and is in fact remarkably accurate. The test does not always give definitely positive or negative results, but must be interpreted in the light of experience. If the

shadow of the gall-bladder is of a standard density, regular in outline, homogeneous, and decreases in size after protein or fat food, it may be relied upon by either method to denote a normal organ. If definite and persistent negative shadows are found, the gall-bladder almost certainly contains stones. If the shadow is faint or absent by the oral method, a supposition of abnormality must be confirmed or disproved by the intravenous method; and if by the intravenous method no shadow is obtained, an additional diagnosis

FIG. 3A. Normal gall-bladder showing a concavity toward the midline.

FIG. 3B. Same patient after barium meal, showing displacement of the gall-bladder to the right by barium-filled stomach and duodenum, with pressure deformity of the gall-bladder, causing the concavity.

of blocked cystic dust may reasonably be made, provided the salt is visible in the colon.* Faintness of the shadow as an evidence of impaired function is reliable only with the intravenous method because of the uncertainty of absorption of the salt from the intestinal tract when given by mouth. We would recommend, therefore, that in ambulatory cases the oral method be employed, accepting as reliable only the normal shadows and those demonstrating calculi; the others should be confirmed by intravenous injection before expressing an opinion as to the presence or absence of pathology. Variations in the size, shape or position of the shadow are only occasionally of value, and should be used cautiously. Variations in the response to food (rate of emptying) occur with fair frequency. Their interpretation in terms of pathology is difficult, but a prompt response is of value in determining the normal.

Our mistakes at first were made in trying to interpret variations in size, shape, position and contour, but these changes were soon found to be of minor importance. The significance of delay in emptying or a weak response to stimulation by food is yet to be determined. The value of any statistics on this subject, however, may be *nil* unless the criteria by which a diagnosis is confirmed be plainly stated. When stones are found, there is no argument. But "cholecystitis" may mean much or little, depending on the pathologist. For instance, Carman reports that in his clinic only 17 "normal" gall-bladders were found in 5,000 examined histologically. It is

* The colon is frequently outlined by the opaque salt in the roentgenograms taken twelve or fifteen hours after intravenous injection.

obvious that anyone's percentage of accuracy would be quite high if all gall-bladders were tagged "cholecystitis," even without this test, providing this same pathologist were consulted. It is obvious, also, that the surgeon will be more prone to explore the patients whose cholecystographic results coincide with their clinical findings, thus giving unbalanced statistical results. In respect to a diagnosis of cholecystitis, this test is, therefore, of immense value. We observe the *function* of the gall-bladder and do not simply inspect its anatomy and structure. Of what importance is an area of round cell infiltration, providing the gall-bladder fills readily, concentrates the bile, and delivers it on demand? In short, we suggest that study should be directed toward the *physiology* of this organ and not alone toward its histological structure. If by this test we are enabled to reveal a "non-functioning gall-bladder" we are then using our resources to the utmost, and the decision for or against surgical intervention should depend upon this function, other things being equal. It is quite similar to the phenolphthalein test of kidney function, and is, in fact, an offspring of that same test, going back to Abel and Rowntree,[11] and even to Remsen.

FIG. 4A. Oral method. Normal gall-bladder shadow at fifteen hours.

FIG. 4B. No change one hour after glucose by mouth.

FIG. 4C. Decrease in size one hour after mixed meal.

The untoward reactions in the intravenous group have in our experience been infrequent, occurring in only 8 per cent of the cases, and, when present have been mild. They include malaise, chills, headache, backache, slight nausea and a feeling of lassitude. One intelligent patient expressed himself thus, "I felt as if I had the grippe for about an hour after the injection." In only one instance did the symptoms necessitate a hypodermic injection of adrenalin, and only one patient suffered a local reaction at the site of injection. (This was an erysipeloid process, apparently due to a leakage of the solution into the tissues around the vein, and cleared up in a week following hot local applications.)

With the oral method mild reactions were rather common and included nausea, vomiting and diarrhea in the following percentages:

	Per Cent
Nausea alone	8.5
Vomiting	8.5
Vomiting and diarrhea	15.0
Diarrhea alone	30.0
No reaction	38.0
Total	100.0

Many of the diarrheas were mild, and frequently the patients felt better after "a single loose movement." They are included, however, as showing evidences of gastrointestinal irritation, which it is hoped may in time be obviated. There was a marked variation from time to time in the reactions, possibly due in part to the numerous changes made in the preparation and composition of the pills or

capsules, but the variation in response to any one preparation was also present, probably indicating individual differences in susceptibility. In only 2 out of the 243 cases were the reactions severe enough to prevent the patients from coming to the hospital for examination the following day.

No definite contraindications have been encountered so far for either method. The tests have been successfully employed in patients with jaundice, cirrhosis of the liver, hemachromatosis, chronic passive congestion, nephritis, hypertension, chronic myocarditis, angina pectoris and brain tumors. Courage to make these trials was born of the discovery that in dogs only a slight increase of the toxicity of the drug was evident in the presence of common bile-duct obstruction or even when half of the hepatic lobules had been destroyed by poisoning with chloroform.*

Findings incidentally made during this series of examinations may be of interest.

1. Six patients had been subjected to cholecystotomy with removal of calculi at various periods before the test, the shortest interval being six months. Five of them presented persistently faint shadows, indicating faulty powers of concentration, and 3 of these contained negative shadows characteristic of calculi. No shadow was secured in the sixth patient.

2. Gallstones were reported 42 times. In 10 cases they were visible as positive ring shadows (such as can be shown by roentgen rays without cholecystography); in 30 others they were evident as negative shadows (shown only by virtue of the relatively opaque substance around them), and in the remaining 2 cases faint ring shadows were seen only at twenty-four and thirty-six hours respectively, not having been visualized previously. These latter two were visible presumably because a small amount of the salt had been deposited in or on the periphery of the stones.

3. In 3 patients with jaundice, no shadow of the gall-bladder was seen, though at re-examination after disappearance of the jaundice, 2 showed normal shadows. These presumably had catarrhal jaundice. The third showed no shadow and was found at operation to have stones blocking the cystic duct, none being found in the common duct.

4. Three patients who subsequently were found to have duodenal ulcers were examined, and all presented normal gall-bladder shadows. A fourth who had an ulcer presented a faint shadow, found at exploration to be due to a cholecystitis,

FIG. 5A. Oral method. Normal shadow at seventeen hours.

FIG. 5B. Decrease in diameter twenty-five minutes after peptones by mouth. (No further change in two hours.)

FIG. 5C. Second decrease in size forty-five minutes after a mixed meal.

* It was uniformly found, however, that no shadows could be obtained in dogs after obstruction of the common bile duct, nor after the destruction by chloroform of more than one-half of the liver lobules.

and not due to secondary involvement by adhesions.

5. Several shadows which showed concave deformities toward the midline were found, on giving barium by mouth, to be due to pressure from a normal duodenum. No pressure defects in the duodenum were seen.

6. In several patients, faint shadows suggesting the outline of a gall-bladder appeared on the plain films. Cholecystograms showed no constant relation between these and the opaque gall-bladder shadow.

8. One gall-bladder noted as "faint and deformed" was found to be normal at operation but compressed by a dilated duodenum, in turn due to an aberrant mesenteric artery. In no case have we found adhesions alone preventing the gall-bladder from filling.

9. Forty-three supposedly normal subjects (medical students, interns and nurses) were examined by the oral method, normal

FIG. 6A. Intravenous method. Normal gall-bladder at 10½ hours.

FIG. 6B. Decrease in size one hour after fat (patient had a gastroenterostomy, no food going through the pylorus).

However, we have frequently noted marked changes in the position of a gall-bladder at interval examinations, as well as in its size, shape and contour, especially after food, so that this check on one of the "indirect" signs is not reliable.

7. Two patients who had presented fairly typical attacks of angina pectoris showed "negative" shadows after the test, and had no unusual reactions from its administration. After cholecystectomy, the supposed angina disappeared in both cases. A third case was found to have a shadow of normal density but a marked delay in emptying, the shadow persisting for thirty-six hours in spite of several full meals. The cause of this is not known as there was no operation.

shadows being obtained in 33 and faint shadows in 10—further evidence that faintness of the gall-bladder shadow is not a reliable index of pathology when the oral administration is employed.

Cholecystography is more accurate in one particular than either the barium meal or pyelography, in that it not only reveals the anatomy and pathology of the gall-bladder, but also throws light on its physiological processes. Believing the function of the gall-bladder to be (*a*) storage (an obvious function); (*b*) concentration (as shown by Rous and McMaster,[12] and others), and (*c*) the delivery of bile to the

duodenum upon proper stimulus as shown by Boyden[13] and ourselves, we have here a method of testing all three functions.

But a more peaceful pursuit than that of selecting erring gall-bladders for the surgeon has been opened to us by Graham's discovery. By it we are able to study the normal physiological reaction of the gall-bladder to various stimuli, and to confirm or disprove some of the results obtained by physiologists in their experiments on animals. Graham's original dicta stated that the patient should not be given any food during the test, and in our series, in a patient who was inadvertently given a full meal, a prompt decrease in the size of the shadow was noted. This seemed to be good evidence that the gall-bladder had emptied its contents into the duodenum, which, if true, would be an important finding, inasmuch as several observers, notably Sweet,[14] and Halpert[15] have stated that the gall-bladder does not empty through the cystic duct but rather by absorption. Experiments were then made to determine what property or element of the food caused this reduction of the shadow. Psychic tests, i. e., the sight, smell or taste of food had no effect, but ingestion of food rich in fat was nearly always followed by a decrease in the size of the shadow with eventual disappearance in three to six hours. It was found that a carbohydrate meal could be given without any effect, that proteins (lean beefsteak) and peptones (Witte's peptone) caused a moderate decrease in the size of the shadow, and that fats, such as butter, cream or egg-yolk gave a marked response. Raw egg albumen caused no decrease in the size of the shadow, but partly coagulated albumen ("soft-boiled") produced slight reduction. Pure olive oil in man had no definite power to empty the gall-bladder, but in dogs its ingestion was followed by a good response. Olive oil treated with the Alpine lamp for one hour gave only a slightly greater response than raw olive oil, probably within the limits of experimental error. Castor oil produced no effect.

With Dr. Cannon's help, we secured a group of volunteers from the first-year class of medical students and pursued investigations along this line, trying various drugs both orally and hypodermically. It was found that there was no constant reaction to drugs, with the exception possibly of magnesium sulphate by duodenal tube, which, as Silverman and Menville[16] had previously shown, caused a moderate decrease in size, comparable to that obtained by proteins and peptones orally. Sodium bicarbonate by mouth, was followed by a slight increase in size of the gall-bladder shadow with a decrease in density. Atropine sulphate by hypodermic injection seemed to have a slight inhibitory effect on the response to food, but there was no direct action on the gall-bladder. Physostigmin, pilocarpin, pituitrin and adrenalin given by hypodermic injection, dilute hydrochloric acid administered orally and by duodenal tube, and nitroglycerin, meat extracts, ginger, starch, sugar, glucose and various other substances given by mouth had no constant effect on either the size or density of the shadow. In dogs, however, a large dose of sodium taurocholate (which according to Whipple[17] is the only effective cholagogue) was followed by an increase in size without a decrease in the density of the gall-bladder shadow.

Alcohol given orally served to rekindle the waning enthusiasm among the students who were volunteering for the test, some of whom suffered from purgation and others from the duodenal tube. As a drug it produced no constant effect on the gall-bladder shadow.

Mechanical factors were then considered and, in an attempt to empty the gall-bladder by increasing the intra-abdominal pressure, a series of exercises involving strenuous use of the abdominal muscles were prescribed for several of the students. Again no effect on the gall-bladder shadow was noted. In view of Winkelstein's findings[18] the tests were repeated, after atropine to physiological saturation had been given, but with the same negative result, throwing doubt upon the correctness of his impression that after supposed paralysis of the sphincter of Oddi by atropine, increased intra-abdominal pressure empties the gall-bladder. It is possible, of course, that the atropine did not act in the desired manner. Likewise, forced respi-

ration, heat and cold (internally and externally), and direct pressure had no effect. However, the irritation of a duodenal tube in an excitable subject was followed by a moderate decrease in size of the shadow, which might have been due to the retching and gagging indulged in by the student.

The explanation of these findings is difficult. It seems clear that the gall-bladder empties to a degree which depends upon the stimulus, and that intra-abdominal pressure alone has no demonstrable part in the emptying. Likewise that drugs, as far as observed, have no constant effect, an observation which seems to prove that a nervous reflex is not a factor. Furthermore, completely de-nervated gall-bladders (in dogs) have shown, after recovery of the animal from the operation, a normal response to the ingestion of fat. Vagus stimulation of varied strength likewise failed to show any change in the size of the gall-bladder shadow, although it produced violent intestinal peristalsis. Direct stimulation of the papilla of Vater by food was considered a factor in the emptying of the gall-bladder until it was found that a maximum contraction was obtained in each of two subjects and three dogs who had functioning gastrojejunostomies, one of the subjects and all of the dogs having had a transection of the pylorus,—effectively short-circuiting the duodenum. This observation was also against the theory of passive or purely hydrostatic emptying by siphonage or suction, as is the variation in response to the different substances injected into the duodenum by tube (e.g. peptone, magnesium sulphate, acids, alkalis and carbohydrates). A circulating hormone as the cause of emptying was then considered and "secretin" (freed from its associated depressor substance) was used in 4 dogs. In 3 of them a questionable decrease in size of the gall-bladder shadow was noted; in the fourth, no effect was observed, after repeated intravenous injections, to the point of marked salivation. Furthermore, dilute hydrochloric acid (which, according to Bayliss and Starling,[19] causes the liberation or formation of secretin on coming in contact with the duodenal mucosa) had no effect on the gall-bladder shadows of either humans or dogs. In short, we have found no rational explanation of the mechanism of response. The important question of active contraction versus passive emptying is also unsettled. Nor have we been able to throw any light on an observation noted by many,—that with a decrease in size of the gall-bladder shadow after food there is an increase in the density, out of proportion to the time factor and in spite of a considerable loss of the shadow-casting substance. Two important facts in relation to the production of a normal shadow have been established, (*a*) that an intact sphincter of Oddi is necessary to obtain a normal cholecystogram. Cannulas were put through the papilla, sewed in place, and after recovery of the animal from the operation, cholecystograms were attempted by the usual technique, but normal shadows could not be otained. Very small shadows suggesting collapsed gall-bladders were seen in 3 dogs, and no shadows were obtained in 4 others; (*b*) that the normal mucosa is important, for no shadow could be obtained for several days after the gall-bladder was curetted. These and other points will be taken up in a later paper.

This preliminary report is given out primarily to show the value of cholecystography to the physiologist and to the student interested in research problems, as well as to the clinician and surgeon. The findings herein reported may serve to explain why patients with gall-bladder disease, especially calculi, avoid fats, and, if the apparent "relaxation" of the gall-bladder after sodium bicarbonate is found to be constant, why they obtain relief from ingestion of alkaline substances. There are many interesting vistas which have been opened to us and we are at present trying to get closer views and more accurate knowledge of some of them.

SUMMARY

(1) The intravenous administration of sodium tetraiodophenolphthalein is a very accurate and reliable test for a non-functioning or poorly functioning gall-bladder, being found reliable in 93.5 per cent of proved cases in our clinic. It is quite safe

if used in the dose and by the technique recommended.

(2) The oral administration is much easier, but gives more frequent reactions and is not so reliable. Its chief value is in ruling out definitely normal gall-bladders and in revealing a certain percentage of non-opaque calculi. If the gall-bladder shadow is faint or absent by this method, the patient should have the added security of confirmation by the intravenous method.

(3) Cholecystography is a valuable method in the study of the physiology of the normal gall-bladder. By this method it has been determined that the gall-bladder empties its contents into the duodenum in response to the ingestion of food, and to a degree which depends upon the chemical constituents of the food.

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FURTHER DEVELOPMENT IN THE JEJUNAL AND ORAL ADMINISTRATION OF THE TETRAIODOPHENOLPHTHALEIN SODIUM SALT*

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IT affords us considerable gratification to have another opportunity to acknowledge the debt of gratitude which roentgenology owes to Dr. Graham and his co-workers for their wonderful discovery and development of cholecystography. Up to the time when their original communication appeared, roentgenography of the gall-bladder had been more or less unsatisfactory. Improvements in apparatus and technique largely accounted for our advancement in diagnosis but there still remained a high percentage of cases in which gall-bladder lesions could not be recognized by roentgen rays. In the visualization of the gall-bladder by means of the Graham test we now know that we have a method at our disposal which will greatly improve the diagnostic value of roentgenography of the gall-bladder.

Our early experiences with the intravenous use of tetrabromphenolphthalein were so disastrous that we were forced to discontinue the method. This was largely due to the sharp reaction experienced by many patients after the injection; some of them were for a time in a critical condition. The symptoms were largely toxic in character. In addition there was the danger of phlebitis from the injection and sloughing of the soft tissues of the arm should a drop or two of the solution escape from the needle during the procedure.

In their article in the January, 1925, issue of Surgery, Gynecology and Obstetrics, Whitaker and Milliken of Boston convinced us that the same roentgenological results could be obtained from tetraiodophenolphthalein in much smaller doses than we had been using with the tetrabrom. The toxicity of the drugs is much the same but because of the small amount of the tetraiodo required there was less systemic reaction when administered intravenously than when tetrabrom was used. A goodly percentage, however, still showed unpleasant symptoms, so much so, that in hospitals with which we are connected it was not deemed advisable to continue the intravenous injections except when all other methods of diagnosis had failed.

In February, 1925, at the suggestion of Dr. Max Einhorn, the authors began to administer the tetraiodophenolphthalein directly into the jejunum through the duodenal tube. It has been tried in a series of 40 cases with most gratifying results. The gall-bladder is, as a rule, clearly outlined and shows a sequence in normal cases much the same as following the intravenous injection, namely, most distended four to five hours after giving the dye, gradually lessening in size and becoming more distinct from the eighth to the twenty-fourth hour, usually disappearing thirty-six hours after the injection.

Some reaction, such as faintness, vomiting and diarrhea appeared in a number of cases. These symptoms, as a rule, occurred about one to one and one-half hours after the injection. They lasted but a short time, when the patient claimed to feel as well as ever.

On account of its being a hospital procedure this method of examination was reserved for those cases undergoing duodenal feeding or non-surgical biliary drainage.

The details of the jejunal injection are as follows: In the early morning the exact position of the tip of the duodenal tube is ascertained roentgenoscopically. If it is well down in the jejunum so that no gastric regurgitation will occur, the examination proceeds. At 6.30 A.M. 300 c.c. of warm milk to which a little cream has been added is given. This partially or completely empties the gall-bladder. At 8 A.M. 30 to 40 grains of tetraiodophenolphthalein dissolved in 300 c.c. of freshly distilled water is slowly injected, usually in two doses, until the full amount has

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been given, the dosage depending upon the weight of the patient (in the average individual of 150 lb., 30 grains is sufficient). Roentgenographic observations are then made 4, 8, 24 and 36 hours after the administration.

Not being entirely satisfied with the results of the jejunal method, particularly on account of the occasional severe reaction and the necessity of hospitalizing the patient, investigations were made with the oral administration, favorable reports having been made by Sosman, and by Menees and Robinson. Salol coated pills or capsules, as recommended at the time by Sosman did not especially appeal to us, mostly on account of the danger of poisoning, and we had great difficulty in satisfactorily formalizing capsules as Menees and Robinson had suggested. What we needed was a safe and reliable enteric coating which would not dissolve in the stomach. Keratin was suggested by our local hospital pharmacist and the results have been such as never to call for a change. We have been using 5 grain keratin coated pills for more than six months with entire satisfaction, the only difficulty being that it has been necessary for us to make them up fresh for each dose. Such a pill-making job in the roentgen department was an almost impossible task. Experience taught us that the moment the pills became hard and dry they were likely to go through the intestinal tract without breaking up. This has been the trouble with the stearic acid coated pills. If the mass was too moist the coating chipped off; if dry, as is necessary for the permanency of this sort of covering, many passed through without disintegrating. In justice to the manufacturers of these commercial pills, however, it must be said that many reliable men are using them apparently with entire satisfaction, the amount of the drug given being large enough to allow for such an occurrence as described above.

Through the kindness of one of our pharmaceutical friends we are now able to obtain capsules coated with resins, each containing 5 grains of tetraiodo. These *seem* to give even more satisfactory results than the pills. Whether they will continue to do so remains to be seen; so far the only objection is the delay in reaching the intestinal tract. In two cases the capsules did not leave the stomach for three to four hours. This is rather unsatisfactory, as it allows time for possible breaking up in the stomach with gastric irritation. At this point it may not be amiss to say something about the drug itself. Tetraiodophenolphthalein is a very unstable drug. It deteriorates rapidly on exposure to light and air. When this occurs it no longer is of use in cholecystography. We have learned this by bitter experience, having had to discard more than one supply of the drug. We are more and more convinced that much of the toxicity is due to impurities and to the result of rapid oxidation. The manufacturers who are making this dye are fully aware of these imperfections. In the July-August issue of the X-Ray Bulletin the Eastman Kodak Company states: "The iodine salt is an extremely difficult chemical to manufacture free of impurities which appear to affect both its opacity to the *x*-rays, its toxicity and its keeping qualities."

It is evident that all chemists interested in this substance are making efforts to give us a pure and stable product. When this occurs many of the objections to the Graham test will be removed.

The capsules that we are now using are rapidly filled with the fresh drug in a darkened room and immediately hermetically sealed with the enteric coating. This prevents, in a large measure, deterioration from the effects of air. They should always be kept in a receptacle which will protect them from light.

There is ample evidence that the dose of the dye generally recommended is too great. One case recently examined showed definite gall-bladder detail with the oral administration of only 15 grains of tetraiodo. For this reason we have gradually reduced our dose so that an average adult weighing 150 lb. receives only 40 grains.

We now routinely use the oral method in all gall-bladder cases referred to our office. It is simple and efficient. The worst than can happen is nausea, vomiting and diarrhea. These complications only occa-

sionally occur and are never of a serious nature. The method of procedure is as follows:

After a thorough cleansing of the intestinal tract, preferably with compound licorice powder given the night before followed by a simple enema in the morning, a preliminary examination of the gall-bladder is made in the ordinary manner at about 10 A.M. The usual lunch is then allowed. At 6.30 P.M. the following meal is advised: a thick soup, creamed chicken, baked potato, bread and butter and a glass of milk. The abundance of fat in this food will partially or completely empty the gall-bladder in from one to two hours. It is then in a receptive condition for the opaque bile. Commencing at 9 P.M. two enteric capsules containing 5 grains each of tetraiodophenolphthalein are given with a wineglass of water every fifteen minutes until 8 capsules are taken. The patient reports at the office twelve hours later, at 9 A.M. the following morning, with an empty stomach, no breakfast being allowed. A series of roentgenograms is then taken. Four hours later, at 1 P.M., the examination is repeated. Regular lunch is allowed at 1:30 followed by a re-examination an hour later. The patient reports the following morning for a final observation.

It is essential to make a preliminary examination before the administration of tetraiodophenolphthalein in order to exclude any lesion which may be overshadowed by the opaque bile. The starvation diet is necessary in order that the gall-bladder may become fully distended when the first roentgen examination is made.

FIG. 1. Oral method. Twelve hours after 35 grains of tetraiodophenolphthalein. Preliminary examination negative. Note mottling from small stones. Well outlined by the dye. Operative findings: Thickened gall-bladder filled with small stones.

FIG. 2. Oral method. Sixteen hours after 40 grains of tetraiodophenolphthalein. Note gall-bladder outlined and packed with stones, many of them showing as negative shadows. Operative findings: Thickened gall-bladder filled with stones.

In normal cases the shadow should appear at the twelfth hour, should slightly diminish in size and become more intense in outline four hours later; as soon as food has been given it should further diminish in size and detail or completely disappear. The following morning, thirty-six hours after the tetraiodo, there should be no shadow present.

Up to the present time our series numbers 147 cases. In not one have we had a severe reaction. One highly hys-

terical patient fainted, 11 had diarrhea, 17 felt nauseated, 12 vomited. Some patients, a very low percentage, complained of feeling depressed and weak. This, however, soon passed away.

In the interpretation of cholecystograms one may readily divide the shadows into those giving direct evidence and those giving indirect evidence of pathology of the gall-bladder.

The first and most important of the direct signs is the actual visualization roentgenographically of nonopaque gall-

FIG. 3. Oral method. Sixteen hours after 40 grains of tetraiodophenolphthalein. Note the roentgenographic evidence of deformity of the gall-bladder shadow. Operative findings: Thickened gall-bladder deformed by omental adhesions.

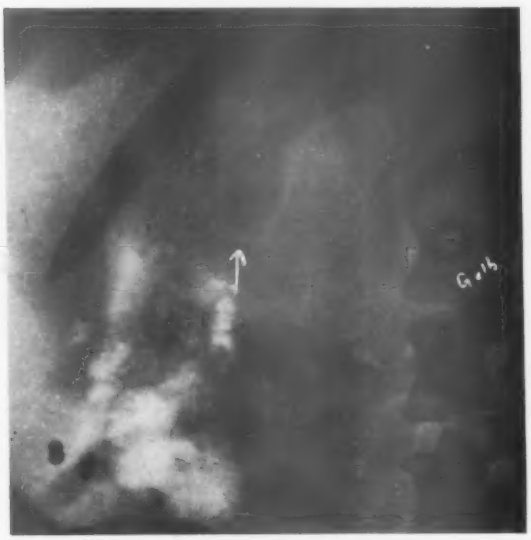

FIG. 4. Oral method. Thirty-six hours after 40 grains of tetraiodophenolphthalein. Late appearance of shadows indicates impaired gall-bladder function from chronic cholecystitis. Roentgen findings verified at time of operation. No obstruction.

stones. These stones are, as a rule, outlined by being surrounded with the opaque bile. In some instances the roughened surface of the stones may absorb a sufficient amount of the dye to become visible in the roentgenograms. It is a noticeable fact that the shadows of gallstones are often brought out into clearer detail after tetraiodophenolphthalein, even though the gall-bladder is not outlined. Mottling of the gall-bladder shadow, as a rule, indicates small stones. One should be exceedingly careful in the interpretation of this sign, for intestinal gas overlapping the gall-bladder shadow may produce this effect. If a painstaking examination is made however, it will be noticed that the small round negative shadows extend beyond the gall-bladder outline.

It must not be construed from the above that all gallstones will be visualized by the test. In a number of cases where pathology of the gall-bladder was reported the surgeon at operation found not only a thickened gall-bladder but stones as well. The explanation is not entirely clear at the present time; it may be due to overshadowing. Most of these cases showed a contracted shadow with roughness of outline.

The second direct sign is deformity of outline caused by adhesions. This is a very reliable finding and is seen quite frequently; one must be sure that it is persistent and not due to pressure. In at least two cases the greatest deformity was noted at the sixteenth hour when concentration was at its highest. The regular sequence indicating the function was apparently not interfered with. The diagnosis was confirmed surgically in both cases.

Moore in the June, 1925, issue of the American Journal of Roentgenology and Radium Therapy states: "As to distortion of outline by adhesions, it may be laid down as almost axiomatic that adhesions about a hollow viscus produce such results only in the rarest of instances. Adhesions fix an organ, occasionally they displace, but only exceptionally do they deform it." This has not been our experience. In numerous instances recognition of deformity by adhesions has been verified by surgical investigation.

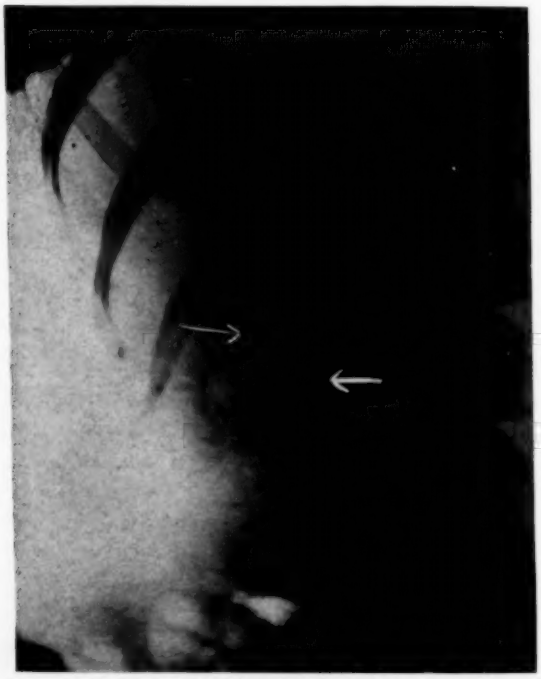

FIG. 5. Oral method. Sixteen hours after 40 grains of tetraiodophenolphthalein. No shadows seen before Graham test. Roentgenographic findings: At least four large gallstones can be recognized. A number of small ones can be seen in the lowest portion of the gall-bladder. Gall-bladder outline faint—evidently some obstruction to the cystic duct preventing free entrance of opaque bile. Surgical findings: Gall-bladder contained four large gallstones, one impacted in the cystic duct. Thirteen small angular facetted stones were found in the fundus of the gall-bladder. Gall-bladder thickened, no adhesions.

In the authors' opinion the indirect signs of pathology of the gall-bladder may be enumerated in their order of importance as follows: (1) absence of shadow; (2) the late appearance of the shadow; (3) persistency of the size of the shadow, and (4) faintness of shadow.

It was early recognized that if the gall-bladder shadow did not appear at any time during the entire series of observations after the administration of tetraiodophenolphthalein, it was in the vast majority of cases due to some obstruction preventing the opaque bile from entering the gall-bladder. This obstruction may be intrinsic or extrinsic. The most common intrinsic obstructions in order of their frequency are the presence of a stone in

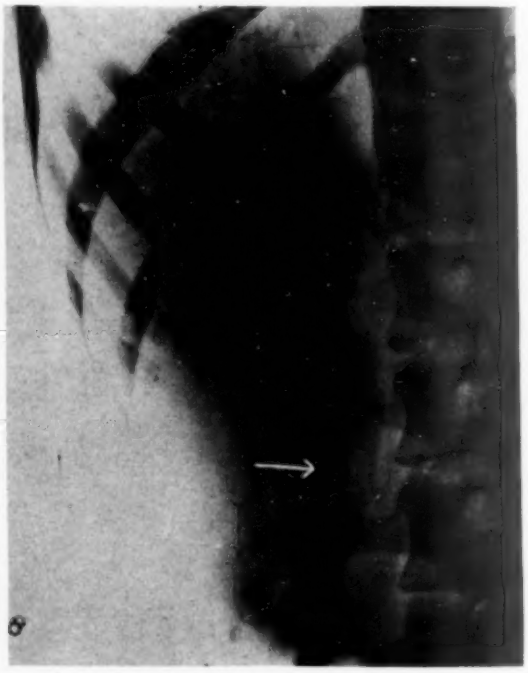

FIG. 6. Oral method. Sixteen hours after 30 grains of tetraiodophenolphthalein. Note shadow of single nonopaque gallstone in elongated gall-bladder, outlined by the surrounding opaque bile—verified.

and stricture of the cystic duct; a swollen mucous membrane may also prevent gall-bladder filling.

The extrinsic causes of obstruction are largely pressure upon the cystic duct by a tumor growth, adhesions or nephrolithiasis. Other causes which prevent the opaque bile from entering the gall-bladder may be briefly enumerated as follows: Obliteration of the lumen of the gall-bladder by shrinkage, polypi or packing with calculi; filling of the gall-bladder with "bile mud" sufficient to prevent entrance of the fresh test bile, and thickening of the walls of the gall-bladder to such an

extent as to prevent a shadow. It is also claimed that a defective liver function may cause such a scantiness of bile that the gall-bladder will not fill; finally, the concentrating power of the gall-bladder may be so interfered with by pathology that the bile is too dilute to cause a shadow. In none of the above causes should we theoretically have jaundice.

If jaundice is present with "no shadow" it will probably be due to a shrunken,

FIG. 7. Oral method. Twelve hours after 15 *grains* of tetraiodophenolphthalein. (Patient refused to take more.) Note definite gall-bladder outline after such a small amount of dye.

contracted and empty gall-bladder due to a chronic intermittent form of obstruction produced by a calculus in the common duct (Courvoisier's law). Other causes are, obstructions above the junction of the cystic duct and common duct, with no bile filling of the gall-bladder, as for example in carcinoma of the hepatic duct or carcinoma of the hilus of the liver; excessive distention of the gall-bladder with bile, in common bile duct obstruction due, for example, to chronic pancreatitis, carcinoma of the head of the pancreas or carcinoma of the papilla of Vater, so that the opaque bile is not sufficiently concentrated to cast a shadow. The surgeons also tell us that we cannot expect a shadow in arrested liver function cases where there has been a very protracted and intense chronic obstructive jaundice due to any cause where the continued back pressure in the biliary system prevents the normal bile from being excreted into the bile ducts or gall-bladder.

It is hoped that a method of analysis may be worked out associating the roent-

FIG. 8. Oral method. Sixteen hours after 40 grains of tetraiodophenolphthalein. Gall-bladder shadow appeared faint and large at the twelfth hour, more distinct and diminished in size at the sixteenth hour, further diminished in size and detail at the eighteenth hour, following lunch. Total disappearance thirty-six hours after tetraiodo—normal sequence for oral method. Surgical findings: Gall-bladder large, walls thin, easily emptied on compression; no stones.

genographic "no shadow" finding with the clinical picture so that we may detect the cause and give the probable location of the lesion. This can only be done by frequent conferences between the roentgenologist, the internist and the surgeon.

If the roentgen finding is "no shadow" it is well to check up on the technique

before rendering a final opinion. It may even require a confirmatory examination. Should there be any question as to whether the capsules or pills have not broken up or the drug lost its opacity, take a 14 x 17 film of the entire abdomen; if fuzzy, flocculent, opaque shadows of tetraiodo can be seen in the intestinal tract you may feel quite certain that the findings are reliable.

The second indirect sign of pathology is the late appearance of the shadow; we have had two cases in our series where the shadow did not appear until thirty-six hours after the tetraiodo was given; both were surgically proven to be pathological. It may be that these findings indicate a delayed concentration of the bile as well as an interference with the emptying power; in both of our verified cases the gall-bladder wall was found to be thickened and in one stones were present which were not recognized roentgenographically.

The third indirect sign, namely, persistency of the size of the shadow of the gall-bladder has not, in our experience, been met with except in one case; the operative findings were a thickened gall-bladder, adhesions and six gallstones. There can be no doubt that such a roentgenographic finding indicates a marked disturbance of function which it is reasonable to consider as due to chronic cholecystitis. More work is necessary on this sign before we can give a satisfactory explanation, although what applies to one case will not at all explain another.

The fourth indirect sign is "faintness of shadow." This is a field into which we have not, up to the present time, dared to venture. There seems to be too much human element entering into the conclusion. If one could standardize the technique and depend upon a constant density in the film it is possible some value might be attached to the findings. Frequently my associates call a shadow faint, when in my judgment it is distinct. There must be something in this interpretation, however, as two of my western friends of large experience claim this finding as one of the most important, irrespective of the fact that one uses tetrabrom by mouth and the other tetraiodo intravenously, the shadows of which vary considerably in intensity. There is however some danger in statistics, particularly a high percentage of positives, if they include cases diagnosed by "faintness of shadow," although if we accept MacCarty's (Mayo Clinic) statement of only 17 normal gall-bladders in 5000 cases almost any percentage would be correct.

There are some extremely interesting problems associated with a recognition of organic disturbance of function; some gall-bladders filled with stones and known to be pathological show a fairly normal filling and emptying of bile. If a disturbance of function indicates pathology, as is claimed by some investigators, when can we roentgenographically consider it surgical? In our opinion only when supported by a clear clinical history calling for surgical relief.

Some of our friends have asked, "What about the cases reported normal in which pathology was found?" In our series we have had very few such cases, and in these the fault was largely in the technique. Some of the interesting physiological problems have already been taken up by Sosman, Whitaker and Edson in their paper on "Clinical and Experimental Cholecystography." We feel, however, that it is necessary in the study of the gall-bladder to recognize the fact that its location, size and function in normal cases depends in a large measure upon the habitus of the patient. In this there is a very close similarity between the gall-bladder and the stomach. One can almost tell by the weight of the patient what sort of a gall-bladder shadow to expect and where it will be located. The time factor must also be seriously considered in the interpretation, for we have no doubt that the gall-bladder is influenced in its function much the same as we see in gastric disturbances of a purely functional nature.

An interesting problem is whether the gall-bladder possesses peristalsis. Our experience with cholecystography would seem to indicate a distinct emptying power of the gall-bladder itself, although we have never been able to recognize peristalsis. This is a field requiring much further investigation before definite conclusions can be reached.

In our enthusiasm over this new method we must not neglect examinations of the gastrointestinal tract. In more than one instance cases have been referred to us for examination of the gall-bladder when the lesion proved to be gastric, duodenal or nephritic. We strongly recommend that all cases submitting to the Graham test should also have a complete gastro-intestinal and kidney examination before arriving at the final findings.

There are other important uses of this test which cannot be overlooked. In the differential diagnosis between cholelithiasis and nephrolithiasis it is much easier on the patient to administer tetraiodo by mouth and obtain a gall-bladder shadow than to do a pyelography and outline the kidney pelvis; in either case one ought to be able to make the differentiation.

It is really wonderful to note how the liver shadow is intensified by the tetraiodo; one can readily recognize enlargements, irregularities and nodulation, especially involving the lower border.

In closing we would like to give a word of warning to those who are recognizing pathology by a visible gall-bladder obtained by the ordinary method. Be careful to check up with the Graham test before expressing a final opinion. Many an interpretation of shadow of a gall-bladder has proven incorrect. This applies as well to supposed pressure defects upon the stomach or first portion of the duodenum by a distended gall-bladder.

ABSTRACT OF DISCUSSION OF PAPERS OF DRS. SOSMAN, STEWART, AND GRAHAM

Dr. Lewis Gregory Cole, New York City. Dr. Cole complimented Dr. Graham and his associates upon the vision and courage which had enabled them to conceive and carry through to a successful termination this very important work on the roentgenology of the gall-bladder. He emphasized the necessity for roentgenologists to thoroughly familiarize themselves with both the roentgenological and pathological findings in the gall-bladder in order that they may have a sound basis for interpretation.

Dr. Cole said that he had hoped much from Dr. Stewart's method of placing the opaque salt directly in the small intestine through a duodenal tube. He asked Dr. Stewart why he had made use of this method in only a relatively small percentage of his cases. Dr. Cole also wished to have information from the pathologists concerning the effect of the various types of pathology of the gall-bladder upon the entrance and exit of bile. He asked Dr. Graham to explain why, if cholecystitis is simply an accompaniment and result of hepatitis, the removal of the gall-bladder, an appendage of the liver, could be depended upon to cure the disease.

Dr. Russell D. Carman, Rochester, Minn. Dr. Carman stated that he had reported 1100 cases in London last July examined by all methods and that since that time his associate, Dr. Moore, had examined 1800 cases, most of them by the oral method. He stated that they prefer the oral method as a routine procedure, checking any obscure cases by the intravenous method.

Dr. James T. Case, Battle Creek, Mich. Dr. Case stated that they had employed the Graham method in about 500 cases, all by the intravenous method. He had found it of use to administer a barium meal during the examination in order to determine the relation of the gall-bladder to the stomach and duodenum. He has found that the indentation in the duodenum formerly thought to be due to pressure of the gall-bladder is, in a considerable number of cases, due to some other cause, such as pressure of an accessory lobe of the liver. He has also seen several bilocular gall-bladders diagnosed by the Graham method and proven at operation. Dr. Case believes that the intravenous method may be considered an office procedure. "The last 350 injections have been done in the office between five and six o'clock and the patients have gone about their affairs. Of that number a few have felt 'grippy' and we have had them lie down on a couch in an adjoining room but they were all able to leave within about a half hour and very few of them made any complaint. I am satisfied that the intravenous method is an office procedure provided the tetraiodo salt is used."

Dr. A. B. Moore, Rochester, Minn., stated that their results have been entirely satisfactory with the oral administration of kerasin coated capsules.

DR. STEWART, in closing, stated in answer to the question of Dr. Cole that he had by no means abandoned the jejunal method of administration. He uses it in the cases that are hospitalized but uses the oral method for office cases.

DR. GRAHAM, closing. One or two questions have been asked, which I should like to try to answer.

I find the first one a little difficult to answer, namely, the one of Dr. Cole. He asks if it is true that if an infection is spread through the liver, how does it happen that removal of the gall-bladder, simply a little appendage of the liver, relieves the patient so frequently.

I suspect that there is perhaps a little implication in this question, that the removal of the gall-bladder very often, or usually, perhaps, does not relieve the patient. Unfortunately, we as surgeons know that there is a good deal of truth in that implication that removal of the gall-bladder, even in outspoken cases of cholecystitis, does not always relieve the patients by any means. We do know, however, that in early cases, removal of the gall-bladder relieves the patient's symptoms; drainage of the gall-bladder accomplishes this in a certain percentage, not nearly as often as the removal of the gall-bladder. Certainly in the old cases, removal of the gall-bladder does not result in the percentage of relief of the patient's symptoms that we get in the early cases.

If the liver is badly damaged, it cannot recover adequately. If, however, we break this vicious circle which goes on always through the lymphatics, between the liver and the gall-bladder, by removal of the gall-bladder, no matter what the explanation is, we certainly can restore most of these individuals to complete health. In all probability the explanation is—although this is merely a guess which, as Mr. Bryan says, all scientists indulge in—that in the liver we are dealing with a structure which is very vascular and which is known to get rid of infections very readily, while in the gall-bladder we are dealing with a structure which is not very vascular and in which, for some inexplicable reason, we are unable to get rid of infections readily. We know that the breaking of the vicious circle by removal of the gall-bladder will give the liver a chance to recover from its infection. If, however, the condition has gone on to the extent of the destruction of much tissue, obviously we cannot cure that patient by removal of the gall-bladder, any more than we can cure a case of tabes dorsalis by curing the active syphilis.

Another question asked was: "Is it necessary to have a damaged mucosa in order to have a failure to get concentration?" That is a question I cannot answer definitely. We know, of course, that concentration of bile depends chiefly upon the limitation of the bile to the gall-bladder. First, the material which is absorbed by the lymphatics must pass out through the mucous membrane. Obviously, then, it stands to reason that if the mucous membrane is replaced by fibrous tissue, concentration will not take place, and also if the lymphatics are thrombosed and diseased, concentration will likewise not take place in a normal way. The fact, however, that these early cases of cholecystitis failed to concentrate the material in the gall-bladder seems to me to speak perhaps more in favor of the idea which I tried to put forth in the early part of my talk, namely, that it is the lymphatics of the gall-bladder which are usually first involved in cases of cholecystitis, and that the failure of concentration in these earlier cases, before the mucous membrane shows much change, is due to the fact that the lymphatics are thrombosed and are no longer as active as normally.

CHOLECYSTOGRAPHY AND OPERATIVE RESULTS IN 182 CASES*

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THE clinical and roentgenologic investigation of affections of the bile passages has made rapid progress in recent months, owing to the introduction of the method of Graham, Cole and Copher, the advantages of which have not yet been properly evaluated.

We desire, first of all, to bring to notice the results of our own experience, with all details that may help in spreading the use of the procedure. A conclusive study is in process of accomplishment, and for our own part we have intensified our work in order to be able to present the complete results of our investigations.

Roentgenologic signs of affections of the bile passages may be direct or indirect. Among the former is the visualization of biliary calculi, the percentage of which, according to the statistics of the Mayo Clinic, reaches a maximum of 38 per cent. Among indirect signs we have those obtained by roentgenologic exploration of the gastrointestinal tract, which are very frequently confusing because of innumerable chronic processes which mask the pathology of the upper right side.

Our first experiments were carried out by the Graham method using sodium tetrabromphenolphthalein. We have had no mishaps of any importance, such as might have dampened our enthusiasm, due to the careful selection of the first cases, made with all the caution which a new procedure demands.

Last January we read an article by Whitaker and Milliken,[1] advocating the use of sodium tetraiodophenolphthalein in place of the earlier dye. Convinced, in advance, of its superiority as a contrast medium for roentgenography and of its far greater safety for the mucous membranes than the tetrabrom compound in its various chemical combinations, we did not hesitate to make use of this new medium in our later investigations. The reasons assigned by Whitaker and Milliken for employing it were based on (1) the comparative opacity of the two salts to the roentgen rays; (2) a comparison of the dosage necessary to produce shadows of the gall-bladder in animals; (3) the comparative toxicity of the two salts and their rate of elimination, and (4) a comparison of their effects in man, all of which considerations led them to conclusions which agree perfectly with our own.

They say that the content in iodin of the sodium tetraiodophenolphthalein is 59 per cent, while the content in bromin of the similar salt is 49 per cent. Since it is known that the atomic weight of iodin is 127 while that of bromin is 80, it is evident that the salt of iodin is approximately twice as opaque to roentgen rays as the salt of bromin, from which it is seen that in practical use 30 per cent less of the salt of iodin is necessary than of that of bromin to obtain the same results in rendering the gall-bladder visible. Experience shows that there is no appreciable difference in the toxicity of the two salts, and the tetraiodophenolphthalein has the further advantage that a wide margin is left for a possible increase of dosage, should this prove necessary, whereas in the case of the tetrabromphenolphthalein salt this would be impossible.

Our first attempts with tetrabromphenolphthalein were made exactly in accordance with the indications laid down by Graham, Cole and Copher. The cases were chosen with the utmost care, with exclusion of a number in whom symptoms of intolerance to the drug had appeared, such as fall in blood pressure, with headache, nausea, vomiting, pain in the back, and sometimes pain in the venous tract. In one case we had a reaction of 3 plus or nearly 4 (differing from the estimation made by Carman and Counsellor of the

[1] WHITAKER, L. R., and MILLIKEN, G. A comparison of sodium tetrabromphenolphthalein with sodium tetraiodophenolphthalein in gall-bladder radiography. *Surg., Gynec. & Obst.*, January, 1925, xl, 17–23.

* Read at the Twenty-sixth Annual Meeting, AMERICAN ROENTGEN RAY SOCIETY, Washington, D. C., Sept. 22–25, 1925.

Mayo Clinic), with a fall of tension to 9 and 4 (Pachon), but all these symptoms disappeared within twenty-four hours, and apparently no trace was left in the organism after the substance was eliminated. The technique followed was that described by the authors of the method.

Notwithstanding all the pains taken in the technique, we determined, in view of the symptoms of intolerance present in some of the patients, to undertake a few more investigations, trying to be still more careful in our selection of cases. The opportunity of using the salt of iodin in our experiments in place of that of bromin filled us with much more enthusiasm, owing to the ease with which the patients tolerate the amount of the iodin salt necessary to make the gall-bladder and the bile ducts visible.

The technique with which we began the first experiments with tetraiodo was the same as that followed with the tetrabrom salt as regards the correct preparation of the gastrointestinal tract, the immediate observation of the patient and the roentgenologic technique. The results were so extremely satisfactory and the tolerance of the patients was so different from that for tetrabrom that in a very small number we had barely perceptible headache with slight nausea and vomiting, without appreciable fall of blood pressure or other symptoms worthy of mention.

Having obtained this picture of tolerance, we began at once to turn our attention to a modification of the technique, which we simplified from day to day until we finally established a method that we use today in all cases.

TECHNIQUE

Preparation of the Patient. A dose of castor oil, 40–50 gm., is administered forty-eight hours before the procedure. The following morning a warm linseed enema (45°C.) is given with a rectal tube, and this is repeated twenty-four hours later. If these means seem insufficient, a saline purgative may be given.

As diet we recommend light porridges of cereal, substances that will not ferment (wheat, tapioca, rice, farina, oatmeal, etc.), beginning these forty-eight hours before the test. Stewed fruits and black coffee are permissible. Milk and other proteins are wholly suspended. This regimen is kept up until 10 P.M. of the night before examination, after which the patient is allowed nothing at all to eat up to the hour of the injection, in order that stomach and duodenum may be perfectly empty. The injection is made between 8.30 and 9 A.M. We take the pulse, temperature, respiration and blood pressure. If the last-named should prove to be below normal we add 0.5 c.c. of a 1:1000 solution of adrenalin to the tetraiodo solution. If the pressure is high, we do not examine the case until the pressure is brought down to normal. At the present time we are using 0.045 gm. of tetraoido per kilo of body weight in a 10 per cent solution in freshly distilled water; we sterilize the solution for fifteen minutes in a hot water bath, and then allow it to cool to a temperature at which the intravenous injection can be made immediately.

THE CHOLECYSTODOSIMETRIC INJECTOR

The technique that we use to carry out cholecystography, the first results of which were presented in the Section of Internal Medicine of the Argentine Medical Association of Buenos Aires (*Rev. Soc. de med. int.*, May, 1925, vi) has been established after use in 50 cases. We have therefore adopted it with some slight modifications of the general technique and certain simplification of points of special technique, indicated by the authors of the method.

Making use of sodium tetraiodophenolphthalein in a 10 to 12 per cent solution, in freshly distilled water and in a quantity never exceeding 40 c.c., we make one single injection by a single puncture of the median vein, on the invariable condition, however, that it shall be done very slowly and with regularity, in order to avoid reactions in the vein which might result from an unsuitable technique.

In the beginning we employed a syringe of 20 to 40 c.c. capacity to make the injection of the solution of the tetraiodo, but as our experience increased we saw that there were serious disadvantages

connected with this, despite the greater care that we had developed in the technique. As the injection requires a period of about fifteen minutes, it is almost impossible to keep the heavy syringe in the vein and at the same time make the injection even and continuous. Such bungling attempts only serve, in most cases, to create complexity at an important and critical moment in the technique and to excite nervous tension in the patient which is detrimental to the ends of the procedure, or, in the majority of cases, to traumatize the veins unduly, as we are obliged to watch every moment to see whether we are within the vein, which needlessly complicates the technique. Moreover, no matter which of the two solutions we use, whether sodium tetraiodophenolphthalein or sodium tetrabromphenolphthalein, either one is very painful when it falls outside of the vein, there being danger that the causticity may produce local necrotic lesions—a result that we had occasion to observe in one of our first cases when we used the syringe as recommended by the authors of the method. Although the final outcome in this case was favorable, there was a good deal of trouble during its course.

In view of considerations of technique that we have gathered in our experience in the many cases in which we have investigated the gall-bladder we have adopted in our recent practice the *cholecysto-dosimetric injector* of our own design, which does away with all the disadvantages of the syringe and simplifies the introduction of the solution in regulated dosage.

Its most important characteristics are its simplicity of technique, its ready sterilization, and its perfect regulation of dosage, as we shall be able to demonstrate, in the description and use of the apparatus.

Description of the Apparatus. The apparatus consists of a graduated glass tube (*A*) with a capacity of 50 c.c., which carries at its upper end a rubber stopper (*B*): this in its turn is pierced by a stopcock (*Y*) which by means of a micrometer screw-plug (*X*) allows communication from the interior of the tube (*A*) with the exterior. To the lower end of the tube (*A*) there is attached a rubber tube, graduated, in accordance with the result of careful study and experimentation, to show the different pressures which the column of fluid must produce in order to measure the dosage and regulate its injection (Fig. 1). This rubber tube, with an internal diameter of 4 mm., carries during its course 2 small control tubes of glass, (*T* and *G*) of the same caliber, which make it possible to see the solution as it passes to the vein.

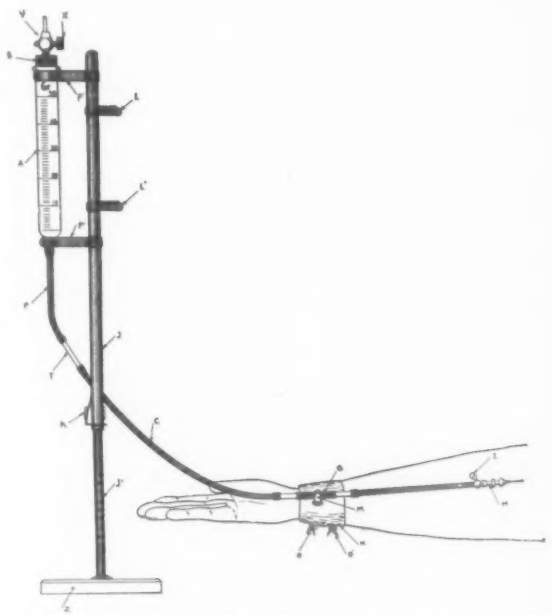

FIG. 1. Model of Saralegui's cholecystodosimetric injector, used in making cholecystograms. A, graduated glass tube; B, rubber stopper; Y, stopcock; X, micrometer screw; T and G, control tubes; H, screw-tip at outlet; I, special shut-off, turning backward and forward; P and P′, brackets for supporting the tube A; J, metal tube telescoping over another tube, J′; K, a sliding elastic stop; L and L′, elastic clips; N, rubber cuff; M, elastic clips for holding the terminal portion of the rubber tube C.

At the lower end of the rubber tube there is a small hollow metal tip (*H*) on which a needle of the usual diameter is mounted, and which is closed by a special shut-off slipping forward and backward (*I*) which greatly facilitates the work of injection when once the needle is introduced into the vein.

The graduated tube (*A*) is held upright by two horizontal supports (*P* and *P′*), which are fixed to a metal tube (*J*) in which another similar tube (*J′*) telescopes; the latter is divided into small horizontal

grooves 1 cm. apart by means of an elastic catch (*K*). This inner tube is the vertical support of the apparatus, and is supported by a removable screw upon a platform of marble (*Z*) sufficiently solid to guarantee stability. Upon the same outer metal tube (*J*) there are two small elastic brackets (*L* and *L'*), which serve to hold the sterile end of the rubber tube and its tip when not in use.

The apparatus also carries a rubber cuff (*N*), 4 fingerbreadths wide, for the purpose

FIG. 2. Roentgenogram showing the venous tract uniformly injected with sodium tetraiodophenolphthalein during the injection made by the cholecystodosimetric injector.

of holding fixed, by means of two small elastic supports (*M*) the rubber conductor with its control tubes. This cuff is placed on the anterior surface of the forearm by means of two small leather straps (*O* and *O'*).

Use of the Apparatus. After sterilizing in the water-bath the two detachable portions of the apparatus, the operator mounts it on its platform, being careful to place the terminal (sterilized) portion, which carries the tip for attaching the needle, within the elastic brackets *L* and *L'*. A small amount of warm physiologic solution is poured into the upper part of the glass tube (*A*), which serves to test the needle and to show whether the apparatus is in working order, care being taken that part of the fluid shall fill the whole rubber tube and part of the glass tube (*A*) as far as the zero mark. This column of fluid will also give assurance whether or not the needle is within the vein at the moment of injection, thus avoiding the possibility of injecting the tetraiodo solution into the subcutaneous tissues. We then turn the sterile, cooled solution of tetraiodophenolphthalein into the same tube (*A*) and close it with its rubber stopper, leaving the regulating micrometer stop-cock slightly open. We are now ready to make the injection.

The cuff is placed on the forearm on the side to be injected, and is so arranged that the distance between the metal supports (*M*) and the site of puncture shall be the same as the distance on the rubber tube from the last glass control tube to the needle attachment. This prevents the needle within the vein from being subjected to any pull during the injection and from being displaced forward or backward, the tip and its attached needle remaining a unit without any danger that some sudden movement of the rubber tube will cause a disconnection and consequent loss of solution (Fig. 2.)

The vein is now immediately punctured by means of a 2 c.c. syringe, and as soon as we are sure that we are in it we detach the syringe from the needle and put in its place the metal tip of the apparatus, which, as we have already stated, has been placed on the flat surface of the forearm where it is held in place by the metallic supports on the cuff. We now open the stop-cock (*I*) of the tip, taking care to do this gently so that the needle will not slip out of the vein. The liquid column of physiologic solution begins to run toward the vein, followed by the blue column of the solution, which is easily seen through the control tubes (*T* and *G*). It can be seen at once whether the physiologic solution falls outside the vein. Once sure that the needle is in the vein, we must regulate the rate at which fluid flows in; this is done by means of the micrometer screw (*X*) in the rubber stopper, or, if necessary, even by raising the level of the solution in the tube (*A*).

As a rule the regulation of the micrometer screw is sufficient to bring about the finest gradations in the velocity with which the fluid enters. In this way it is possible to regulate an injection perfectly and to continue it for as long a period of time as is desired. We employ ten to fifteen minutes, according to the apparent size of the veins of each subject.

When the column of fluid in the last moments of the injection fills only the rubber tube, the pressure diminishes to such a point that it nearly always stops altogether or moves very slowly, in this way making it impossible for air-bubbles to enter the circulation. The stop-cock in the tip is closed, the needle withdrawn, and the usual asepsis of the region carried out.[1]

We have carried out this procedure in 182 cases, without any selection of patients, not even having excluded those with hypertension, those with mitro-aortic disease, or one patient with arrhythmic pulse, and we have had no sign of toxicity or of cardiac depression. However, we believe it is more prudent to desist from injection in these cases and to submit them first to suitable treatment. We have also used this technique in a number of cases of chronic jaundice. The first of these patients was a woman in a grave condition of cachexia in whom jaundice was very intense owing to a cancer of the head of the pancreas. After she was prepared for the injection it could not be carried out on the day set on account of her grave general condition of hypotension, marked cardiac failure and cachectic condition. She was given adrenalin, camphorated oil and physiologic solution by rectum to overcome the serious cardiac symptoms. At the end of eighteen hours it was possible to give the injection of tetraiodo. The patient tolerated it perfectly without any untoward symptoms. In a second case we were dealing with a case of chronic jaundice in a man sixty-five years of age, who had already had a first attack of subacute jaundice a year previous which improved under medical treatment and disappeared within two months. His general condition was good. After receiving the injection this patient was disturbed a number of times during the day in order to make roentgenoscopic exploration of the gall-bladder. Despite this he bore the solution perfectly without any trouble. The third case of chronic jaundice was in a man forty-two years old who had been ill for fourteen months; he was undernourished, with arterial hypotension and in bad general condition. The case looked like one of syphilitic cirrhosis. The injecti on was made, and it was then necessary to move the patient on the same day to make the roentgenograms outside the hospital. Nevertheless he showed perfect tolerance to the solution.

These results make it impossible for us to regard chronic jaundice as a contraindication for performing cholecystography, even in cases which suggest an obstruction of the gall-bladder. But in these cases we reduce the dose of the medicament to 0.040 gm. per kilo of body weight. Nor do we accept any other contraindication, but we advise a complete study of the patient, a very careful preparation and a scrupulous observance of the technique of the injection; he should also be watched carefully for eight hours after the injection is made. All patients are kept quiet and isolated for eight to ten hours, with a view to avoiding the more troublesome symptoms belonging to this period such as headache, nausea, and rarely vomiting, all these symptoms disappearing promptly.

The roentgenograms are made after 5, 8, 24 and 36 hours. We always use the Bucky-Potter diaphragm, 60 ma., 55–60 kv., and a double intensifying screen. All these details of technique have been standardized in our practice, with a view to obtaining roentgenographic images that are uniform for purposes of comparison with similar shadows.

To get certain results it is impossible for the technique to be too scrupulous. Attempts were made to administer the same substance by the gastric route, but we were unable to make capsules whose walls were resistant to the acid media of the stomach and which would be dissolved only in the intestine. Those that we used

[1] In the construction of this apparatus we have have had special cooperation from Mr. Andrés Bezzi, chief laboratory technician of Messrs. Lutz Ferrando and Company, whom we desire to thank for his intelligent assistance.

produced vomiting which caused the elimination of the substance, even when the patients showed no reaction of intolerance. For lack of suitable material we were unable to employ acid-resisting capsules.

RESULTS

Our own experience fully justifies the opinion of the authors of the method as well as that of others who have so far interested themselves in the results obtained and the interpretation of the shadows regarded as a a normal or a pathologic expression of the gall-bladder (Fig. 3).

FIG. 3. *Roentgen-Ray Diagnosis.* Gall-bladder normal and in normal position. Filling and emptying normal. *Results of Operation* (Dr. E. Vila). Gall-bladder free, of normal size and position, the bile ducts free.

We have succeeded in demonstrating that between four and eight hours is the time in which the gall-bladder becomes most clearly visible. Thus it becomes possible to study the position, form, size, emptying time and other special conditions of the gall-bladder and the large bile ducts. After eight hours and up to twenty-four hours the shadow of the gallbladder begins to diminish in size and to lose its sharp outlines. This must be taken into account when the roentgenograms are read, in order to establish the conditions of its normal or pathologic drainage. An apparently healthy gall-bladder may be regarded as such when its shadow is uniformly projected, its outline is regular, its position is normal and its emptying is accomplished within the twenty-four hours following injection (Fig. 4).

Gall-bladders may be pathological without the presence of calculi, and their visualization depends on the patency of the cystic duct. It is evident that if this duct is obstructed it is not possible to get the image of the gall-bladder. Among such cases we include calculous cholecystitis with calculous obstruction of the cystic duct, inflammatory cholecystitis with obstruction due to intravesicular or extravesicular lesion, neoplasms, torsions, etc. In cases where the cystic duct is patent, the roent-

FIG. 4. *Roentgen-Ray Diagnosis.* Gall-bladder of normal size, position higher than normal. Its internal surface modified by the duodenum, which is probably adherent. No gallstones visible, bile ducts free. *Results of Operation* (Dr. A. J. Bengolea). Gall-bladder adherent to the internal face of the liver and duodenum, bound by many smooth, inflammatory adhesions. Inflammatory pericholecystitis. No gallstones no duodenal ulcer. Bile ducts free.

genologic interpretation is more delicate, for here modifications may be observed in the intensity and type of the shadow, its position, form, size and the emptying of the gall-bladder. These will demonstrate the possible existence of calculi, new growths, ulcerations, inspissation of the bile content, adhesions, diminution or loss of elasticity of the walls (Fig. 5).

For proper comparison of the roentgeno. graphic images it is necessary to standardize the technique of the procedure. In this way it becomes possible to establish with great detail a large amount of small

data presented by the different roentgenograms. In cases of chronic inflammation of the gall-bladder it can frequently be seen that the filling and emptying of the organ are retarded, and that after eight hours, when the peristalsis of its walls is studied by means of duodenal excitation (after giving soft food), in cases of atonic gall-bladders they fail to empty (Fig. 6).

Finally a study was made of the action of pituitrin upon the peristalsis of the gall-bladder. A distinct reaction to the drug was observed by the contractions of the gall-bladder. We believe that this finding may have a practical importance for the physiology, pathology and treatment of biliary calculosis. The maximum effect was observed within twenty to thirty minutes.

In some cases in which direct roentgenograms of the gall-bladder have been negative, we have succeeded in establishing the presence of gallstones when these were numerous and in scant bile. These are the cases in which the calculi, becoming clearly outlined by reason of the deposits of opaque substance between them, give the well-known appearance of a honeycomb, which we have been able to see in 6 cases.

In cases of chronic cholecystitis (Fig. 7) with inflammatory adhesions it is easy to see the changes in the form of the gall-bladder, since different views can be taken according to the modifications produced by the inflammatory process. Frequently the films show the gall-badder fixed at the level of the projection of the last rib, and always outside of the normal site, tending to go farther outward every hour as it is observed from the fifth hour on. A shadow often seen is that to which we have given the name of "kettle-shaped gall-bladder," which represents a deformity of the internal surface. At other times when the inflammatory process is more extended, the projection of the organ is seen fixed at the level of the last rib or above it in the form of a glove finger.

Finally, there are lesions outside the bile system which may, through compression, cause various deformities, whose appearance will depend on the relations existing between the gall-bladder and the process. We may cite a single case—one

FIG. 5. *Roentgen-Ray Diagnosis.* Gall-bladder enlarged, adherent to the internal face of the liver. Duodenum visible below it, fixed and turned toward that region. Emptying and filling normal. *Results of Operation* (Dr. E. Vila). Gall-bladder enlarged. Intense pericholecystitis with marked adhesions between gall-bladder and duodenum. No gallstones. No duodenal ulcer. Gall-bladder fluid thick, mucous, its flow retarded.

FIG. 6. *Roentgen-Ray Diagnosis.* Colecystitis with gallstones. Large calculi in the neck of the organ, which was probably the site of an old calculus that has been eliminated. Very little bile. No adhesions. *Results of Operation* (Dr. E. Vila). Cholecystitis with gallstones. Two large single calculi. Upper portion dilated, containing a large amount of thick bile; presumably this has been the site of a large gallstone eliminated by the patient some two years before, after an attack.

that is highly illustrative—of the deformation of the gall-bladder by an hydatid cyst of the lower surface of the liver, which by its pressure had deformed the inner surface of the gall-bladder, the diagnosis being corroborated on surgical interventions (Fig. 8).

Aside from cholecystography, it seemed to us that it might be possible to obtain roentgenographic images of the large extrahepatic bile ducts, and that their visibility would depend on correctness of the details of technique. In fact, upon making such a study, in a colleague, of the roentgenographic images obtained by means of this test, we were able to get an excellent picture of the common duct without the gall-bladder being visible, which suggested an obstruction of the cystic duct with a dilatation of the common duct—both of which conditions were confirmed at operation.

FIG. 7. *Roentgen-Ray Diagnosis.* Gall-bladder filling and emptying normally. A point that draws the attention is its outward flexure and the pointed shape of the base of the organ. No gallstones visible. Position normal. *Results of Operation* (Dr. Caballero). Gall-bladder free at its upper end, which is in good position. No gallstones. Base of gall-bladder smoothly adherent to duodenum. No ulcer. Periduodenitis of the second portion of the duodenum.

FIG. 8. *Roentgen-Ray Diagnosis.* Gall-bladder normal, its internal surface strongly modified by a palpable tumor, which, before roentgen examination, was believed to be an hydropic gall-bladder. It now seems probable that it is a small cyst of the lower surface of the liver. *Results of Operation* (Dr. E. Fox). Hydatid cyst of the lower surface of the liver, of the size of a mandarin, which makes pressure upon the internal surface of the gall-bladder. No adhesions anywhere. Gall-bladder normal, free.

GIANT CELL TUMOR OF MIDDLE THIRD OF SHAFT OF FIBULA

A CASE REPORT*

BY B. R. KIRKLIN, M.D., AND W. D. GATCH, M.D.

MUNCIE, INDIANA INDIANAPOLIS, INDIANA

OUR reason for reporting this case is that giant cell tumors in the shaft of a long bone are very rare. We were informed in February, 1925, by Dr. E. A. Codman, registrar of the Registry of Bone Sarcoma of the American College of Surgeons, that up to that time there had been no such case registered. This case has recently been registered.

FIG. 1. Roentgenogram taken December 9, 1919.

B. R., male, aged four and one-half years, was first seen December 9, 1919, having been referred to one of us (Kirklin) by Dr. L. C. Marshall, Mt. Summit, Indiana, for roentgen examination of suspected fracture of left fibula. The previous day while playing, and without any injury whatsoever, he fell suddenly to the floor. He was unable to walk and suffered considerable pain.

Had tonsillitis frequently in infancy. Tonsils removed at age of four. Pertussis at two and one-half years and measles at three years. No known complications from either. Six months ago was kicked by a playmate on left leg, but no apparent disability resulted. During past few months complained of leg ache occasionally but mother does not remember which leg.

Maternal great-grandmother died of cancer of the face. Paternal aunt died of cancer of face. Father and mother living and in excellent health. Has younger sister in good health.

General physical examination revealed nothing abnormal except for very slight swelling over middle of left fibula, which was very tender. Unable to bear weight on this leg. Roentgen study showed a cyst-like expansion of the middle third of the shaft of the left fibula; the cortex was very thin with pathological fracture through same. The area of expansion

FIG. 2. Roentgenogram taken five and one-half years after resection.

* Read at the Twenty-sixth Annual Meeting, AMERICAN ROENTGEN RAY SOCIETY, Washington, D. C., Sept. 22–25, 1925.

is approximately 5 cm. in length. Roentgen conclusion: Bone tumor middle third of left fibula with pathological fracture. Wassermann reaction negative.

Patient was sent to Robert W. Long Hospital, Indianapolis, and operated on December 23, 1919 by one of us (Gatch) who resected fibula for a distance of 2 cm. above and below expansion caused by tumor. Frozen section diagnosis: Giant cell sarcoma. The wound was cauterized thoroughly with phenol and left open for the application of radium which was made a few days later.

The boy made an uneventful recovery and has enjoyed excellent health since. There is no noticeable deformity of the leg or foot. Present height 57 inches, weight 93 pounds.

Dr. E. Vernon Hahn of the Indiana University School of Medicine made the following pathological report:

Hospital No. 10092 Laboratory No. 1630

Gross specimen: This specimen was more or less mutilated before being brought to the laboratory. The operator stated that a solid mass of friable tissue lay in the cyst-like expansion of bone. The specimen as received in the laboratory consists of 5 cm. of fibula of conical shape. The narrow end is 1 cm. in diameter. At the broadest portion the diameter is 2 cm. The broad end presents a funnel-shaped cavity in the depths of which are shreds and fragments of tissue which is definitely fibrous in places and friable and blood stained in others. Bits of this tissue were taken for histological examination. The bony wall of the funnel-shaped cavity is of paper thinness. The appearance of the inner surface does not suggest that there was a definite cyst.

FIG. 3. Photograph of mutilated gross specimen.

Microscopic Description: The structure varies so much that several different pictures will have to be described separately.

The more striking and characteristic areas consist of a rather loose tissue of cells resembling fibroblasts, among which are scattered numerous giant cells of the epulis type. The intercellular substance is foamy and delicately fibrillar. The giant cells range in size from 80 micra to about 12 micra. Their cytoplasm is basophilic. Their two to fifteen nuclei are oval and about 6 by 8 micra in dimensions. They are rather vesicular and almost all of them contain one or two basophilic granules. There is no regularity in the arrangement of the nuclei within the giant cells. Large mononuclear cells with nuclei identical to the above described are also found in large numbers. There are very few well-formed blood vessels in this tissue but there are numerous clefts and irregular spaces occupied by blood. About some of these blood spaces the giant cells are particularly numerous, constituting almost continuous sheets of syncytium. Some of these giant cell areas have scalloped edges, apparently anatomically determined, and the giant cells are most numerous close to these edges, but are not lacking deep in the tissue.

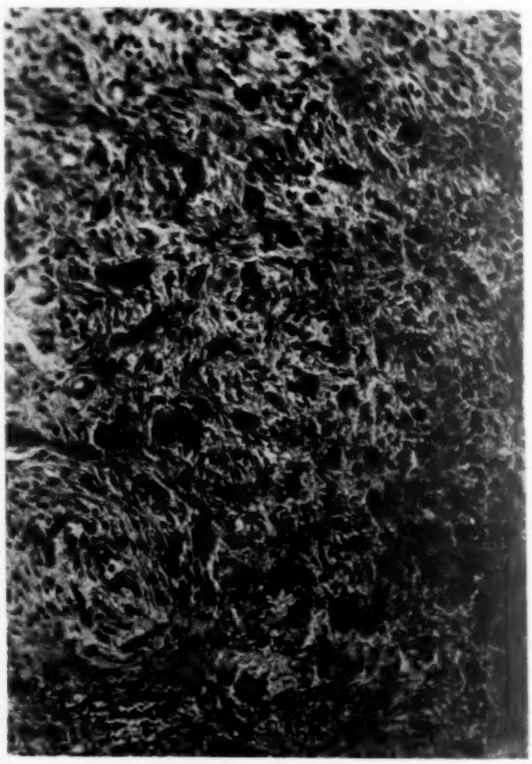

FIG. 4. Photomicrograph showing typical giant cells.

Another type of tissue consists of more or less fasciculated fibroblasts, strands of which

interlace so as to form a lattice-work, the meshes of which are occupied by paler and looser fibrous tissue. The reason for this peculiar structure becomes apparent when this tissue is traced into areas of degenerated blood. Wisps of fibroblasts are seen growing out into the blood clot subdividing it into circular and polygonal areas. The looser, paler fibrous tissue above mentioned clearly results from the subsequent organization of these blood-clot islands. Cystic spaces also occur in this tissue and giant cells are found in the tissue abutting upon them and even lying free within them.

The tissue just described merges into areas of more uniform texture containing spicules of new-formed bone surrounded by large deeply staining osteoblasts. Here there are well-formed blood capillaries. Giant cells in moderate numbers are scattered through the fibrous tissue intervening between the spicules of bone. These giant cells are identical in appearance to those above described and show no significant relationship to the bone. The larger spicules show definite calcification.

Interpretation and Discussion. The preponderating cells above described as resembling fibroblasts show no hyperchromatism or other anaplastic characteristics. None of the giant cells has large, lobed and hyperchromatic nuclei. Therefore the lesion is considered benign. The areas of fibrous tissue without giant cells and with spicules of bone closely resemble solid osteitis fibrosa. The areas rich in giant cells are indistinguishable from benign giant cell tumor. These giant cell areas are closely related to cysts of microscopic size occupied by blood, and to blood-filled tissue clefts. The fibrous areas are clearly the result of the organization of old blood clot, and the areas with bone a still later stage of the repair process. Proliferating tissue rich in giant cells occurring in lesions predominatingly osteitis fibrosa have been interpreted by some pathologists as the result of the fortuitous development of a true neoplasm—a sort of accidental episode in the life history of osteitis fibrosa. No such interpretation can be applicable to this specimen. The giant cell bearing tissue is nowhere circumscribed nor are the giant cells limited to any one part of the lesion. All parts of this tissue strongly suggest a purely reparative reaction. The variation in the histological appearance is due to the different stages of a progressive process and to minutely local conditions which in some places favored the proliferation of fibroblasts and in others the multiplication (or wandering in) of monocytes and their subsequent conversion into giant cells. Specimens more or less like this one, several of which I have seen, provide a link between bone lesions generally regarded as of inflammatory or traumatic origin and "giant cell sarcoma" which has been almost universally regarded as a neoplasm although its benign nature is now well known. The specimen in question is not identical with typical benign giant cell tumor which, however, is said to occur only in the ends of the long bones. The differences between this lesion and typical benign giant cell tumor may reasonably be assumed to be due to the locality in which it developed.

Diagnosis. Benign giant cell tumor of the shaft of the fibula.

BARIUM SULPHATE AS A PROTECTIVE MATERIAL AGAINST ROENTGEN RADIATION*

BY FRANKLIN L. HUNT, PH.D.

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BARIUM sulphate, in the form of bricks and plaster, has been used to some extent as a substitute for metallic lead for protection against roentgen radiation.[1,2] To make a strong serviceable material, the barium sulphate has to be mixed with some binding medium such as glue, shellac, sodium silicate or Portland cement, and frequently layers of cheese cloth or similarly meshed material are embedded in the plaster for additional strength. The advantages claimed are greater facility in applying the material to the walls of roentgen-ray treatment rooms than with metallic lead which, in the form of large sheets, becomes difficult to handle, and also the ability to form the material around objects of irregular shape, such as tube protectors or similar shields. On the other hand, aside from the fact that much thicker layers of the material are required than with metallic lead, there are certain inherent characteristics which should be considered when this material is used. These are discussed in the present investigation.

Samples of barium sulphate plaster, which consisted of a mixture of two parts of coarsely ground and one part finely ground barium sulphate (passed U. S. Standard sieves Nos. 12 and 100 respectively), and one part Portland cement, were prepared in thicknesses varying from 3 mm. (⅛ in.) to 10 mm. (⅜ in.). By piling, these were used to give layers of protective material up to 70 mm. (2¾ in.) in thickness. The protective value of this plaster in terms of that of metallic lead was then determined by placing samples of the material and an echelon, made of strips of lead of different known thicknesses, side by side on a photographic plate, enclosed in a double opaque envelope, and exposing both simultaneously to the unfiltered radiation from a Coolidge tube excited by mechanically rectified alternating current. Care was taken to exclude stray radiation by surrounding the test material and lead echelon with strips of lead, and protecting the photographic plate at the back with a heavy plate of lead. The thickness of the steps of the lead echelons varied from 0.06 to 1.50 mm. For most of the tests the samples of plaster were 3 to 10 mm. thick. The coarsely ground barium sulphate was found by analysis to contain 86 per cent barium sulphate. The impurities were silica and ferric oxide.

A series of measurements of the protective value of the plaster were made with voltages across the tube varying from 50 kilovolts, which was the minimum voltage at which an appreciable amount of roentgen radiation would penetrate plaques of the material 3 mm. thick, to 200 kv. The voltages were determined by measuring the alternate spark gap across the tube between needle points up to 150 kv.[3] and between 12.5 cm. spheres for the remaining voltages up to 200 kv.[4] A universal Coolidge tube was used for the measurements up to 150 kv. and a Coolidge deep therapy tube for the higher voltages.† The current through the tube varied from 4 ma. at 200 kv., to 35 ma. at 50 kv., and exposures from 1 to 30 minutes. For the larger currents, the tube was operated intermittently for periods of 10 seconds to one minute with sufficient time between to allow the tube to cool.

The lead equivalent thickness of the samples was found by determining with a Martens polarization photometer the density of the part of the photographic plate under the barium sulphate plaster and of the two corresponding steps of the lead echelon, one just denser and the other just less dense than the plaster. From the photometer readings and the known thick-

† The author is indebted to Major H. W. Grady, U. S. A., for placing the deep therapy equipment of Walter Reed Hospital, Washington, D. C., at his disposal for measurements above 150 kv.

* Published by Permission of the Director of the National Bureau of Standards of the U. S. Department of Commerce.

ness of the corresponding echelon steps, the equivalent thickness of the sample, in terms of lead, could be obtained by interpolation to 0.01 mm. of lead.

The possibility of soft secondary radiation from the sample fogging the plate and giving an abnormally low value of the protective coefficient was investigated by placing strips of metallic lead from 0.1 mm. to 0.3 mm. thick between some of the specimens and the photographic plate. With thin specimens of the material a detectable effect, due to the secondary radiation, was found. The results, computed from the thicker specimens, however, agreed with those obtained with the strips of lead between the specimen and plate, and were, therefore, used in computing the results. This procedure was considered preferable to using the results obtained through lead since, in practice, relatively thick layers of the material would be used and, moreover, the introduction of lead between the specimen and plate would change the character of the radiation which reached the plate.

It should also be borne in mind that what is sought in this instance is not the absorption coefficient of the material but its protective effect when subjected to heterogeneous roentgen radiation. If an appreciable amount of secondary radiation is produced in the absorbing material and penetrates it, obviously the fact that it is secondary radiation makes no difference from the point of view of protection. If the secondary radiation emitted is sufficiently intense to penetrate an appreciable layer of air, it should be included with the primary radiation in measuring the effect.

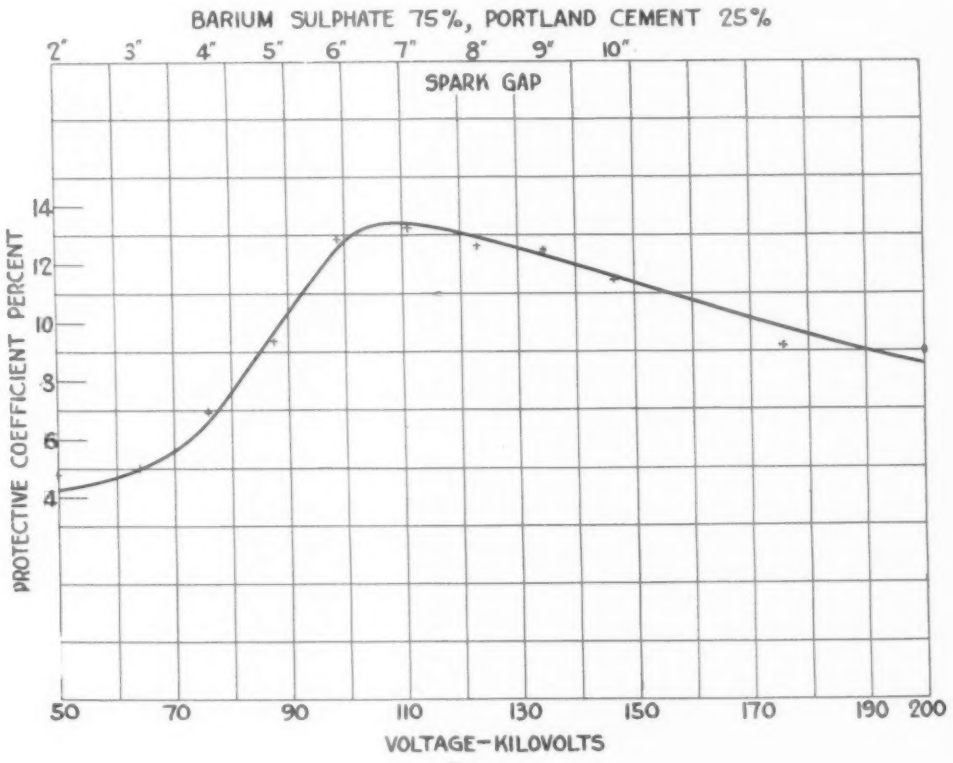

FIG. 1.

The results for the entire voltage range are summarized in Table 1 and shown graphically in Figure 1. Each value of the protective equivalent given is the mean of several independent determinations, but owing to the uncertainty in measuring the voltages by the spark gap method, and to other experimental errors, the protective coefficient may be uncertain from 0.5 to 1 per cent.

The protective coefficient is obtained by dividing the lead equivalent thickness

TABLE 1

PROTECTIVE COEFFICIENT OF BARIUM SULPHATE PLASTER

Spark Gap between Points, Inches	Peak Voltage, Kilovolts	Protective Coefficient, Per Cent
2	50	4.7
3	65	4.9
4	75	6.9
5	85	9.3
6	100	12.8
7	110	13.2
8	120	12.6
9	135	12.5
10	145	11.4
Sphere Gap Cm.		
7.5	175	9.2
9.0	200	9.0

the maximum voltage used. This change is consistent with the known variation with the wave-length of the absorbing power of barium if it be assumed that the hetereogeneous radiation used in the experiments produces in the vicinity of the barium K absorption limit an effect similar to monochromatic radiation. With monochromatic radiation there is a sharp break in the absorption curve, with a large increase in the absorption, when the incident light begins to exceed in frequency the K absorption limit for barium. The less abrupt break in the curve found from these experiments and its displacement toward the higher voltages are undoubtedly due to the hetero-

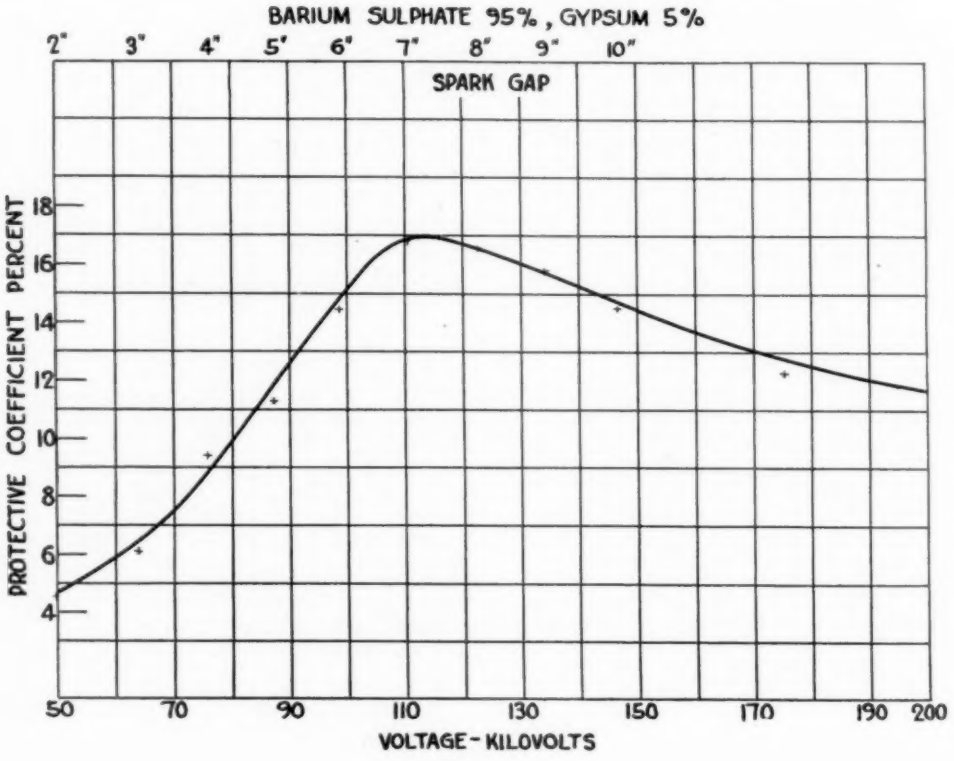

FIG. 2.

by the thickness of the samples, that is, it is the lead equivalent of unit thickness of the material, and is expressed in per cent since it is a ratio which is independent of the thickness of the material.

The large variation in the protective coefficient is evident. At 50 kv. it is only 5 per cent, increases to 13 per cent at 110 kv., and decreases to 9 per cent at 200 kv., geneous nature of the incident roentgen rays.

To make sure that the results on barium sulphate plaster were characteristic of the barium sulphate present and not appreciably affected by the other constituents, the experiments were repeated with identical procedure, using plaques made of pure barium sulphate with the minimum

TABLE II

PROTECTIVE COEFFICIENT OF BARIUM SULPHATE

Spark Gap between Points, Inches	Peak Voltage, Kilovolts	Protective Coefficient, Per Cent
2	50	4.5
3	65	6.1
4	75	9.4
5	85	11.3
6	100	14.4
7	110	16.9
8	120	16.5
9	135	15.8
10	145	14.5
Sphere Gap Cm.		
7.5	175	12.2
9.0	200	12.2

obtained with the plaster, which is consistent, assuming that practically all of the absorption of the plaster is due to the barium sulphate present.

Another characteristic of the barium sulphate plaster brought out by the experiments is its nonhomogeneous, granular structure due to the mixture of relatively transparent Portland cement with coarse grained barium sulphate which gives a porous effect with the result that, unless thick layers of the material are used, roentgen radiation penetrates through and between the granules of the barium sulphate in appreciable amounts. The effect is clearly shown in Figures 3

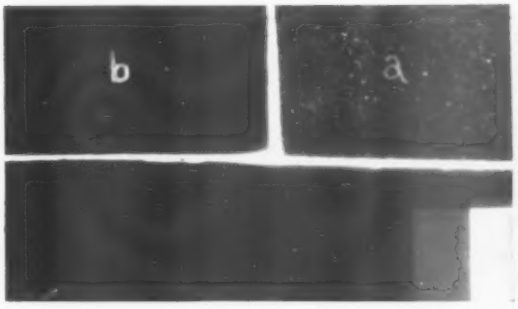

FIG. 3.

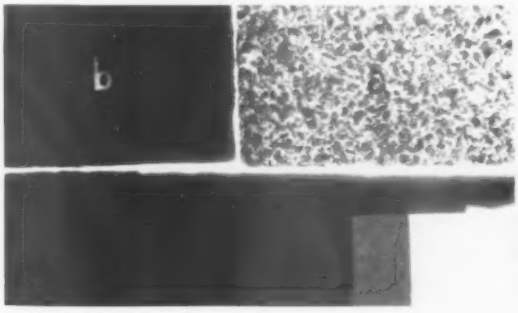

FIG. 4.

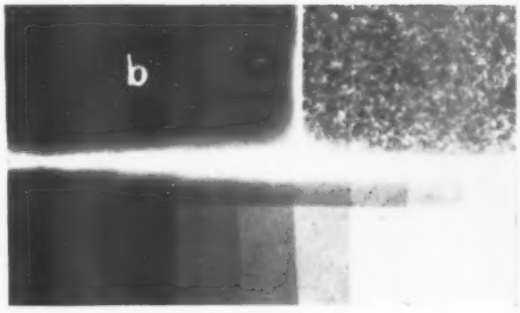

FIG. 5.

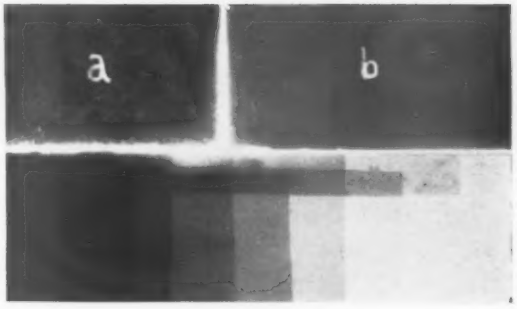

FIG. 6.

amount of gypsum (5 per cent) added which could be used and still have the plaster retain form. This material was much too weak for practical use as plaster but served to verify the first experiments. The results are given in Table II and Figure 2. The curve is of the same form as that obtained with the barium sulphate plaster, and shows the same increase in absorption effect from 50 kv. to 110 kv., and then the decrease to 200 kv. The values are approximately 30 per cent higher than those

to 7, where photographs taken through layers of the plaster from 3 mm. to 38 mm. thick, and voltages from 50 to 200 kv., are shown. For comparison, the corresponding effect through lead echelons are given beside them. A plaque of the finely ground barium sulphate gypsum mixture is also shown in Fig. 6 (*b*) and is seen to be practically homogeneous, thus showing that the lack of uniformity is due to the coarsely ground barium sulphate. Figure 7 is especially significant. It gives a photograph taken

through an echelon of plaster with four steps, each approximately 10 mm. thick, and shows by the mottled appearance of the third step that, with 145 kv. roentgen rays, 10 ma. current, and 10 min. exposure 50 cm. from the focus of the tube, a detectable amount of roentgen radiation still penetrates 28 mm. (1⅛ in.) of the material. A similar test with 200 kv. roentgen rays, current 4 ma., and 30 min. exposure 50 cm. from the focus, shows a slight penetration through 57 mm. (2¼ in.), and a

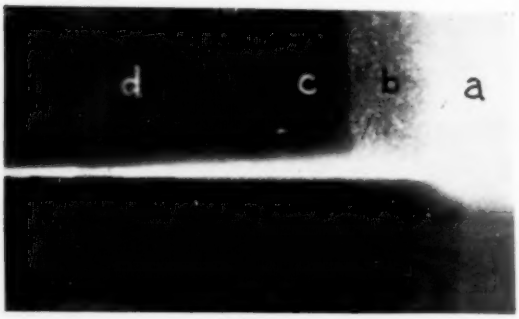

FIG. 7.

third test with 100 kv. roentgen rays, 20 ma. current, 10 min. exposure 50 cm. from the focus showed the same effect through 12.5 mm. (½ in.) of the material. Evidently this is a serious defect, particularly with voltages above 100 kv., and should be overcome either by using thicker layers than would be necessary if the material were homogeneous, or preferably by changing the composition of the plaster.

For complete protection for 100 kv. roentgen radiation, at least 3 mm. of metallic lead are recommended, and for 200 kv. roentgen rays, not less than 6 mm. On this basis, layers of plaster not less than 25 mm. (1 in.) thick should be used for 100 kv. roentgen rays, and not less than 70 mm. (2¾ in.) when 200 kv. equipment is used. In view of the nonhomogeneous nature of the material, as shown by the experiments, these values represent the minimum thickness consistent with safety, and, where practical, somewhat thicker layers are recommended.

The low value of the protective coefficient in the vicinity of 50 kv. offers no practical difficulty provided reasonably thick layers of the material are used; for example, 25 mm. (1 in.) for all voltages below 100 kv. because of the relative ease with which such radiation is absorbed, but if voltages higher than 200 kv. come into general use in the future, it will be necessary to ascertain whether the protective coefficient which decreases constantly from 110 kv. to 200 kv. still continues to decrease for higher voltages and if so to provide, for adequate protection, correspondingly thicker layers of the material than would otherwise be required.

The author wishes to thank Major H. W. Grady, U. S. A., for cooperation in making the measurements above 150 kilovolts, and members of the Bureau of Standards staff for assistance as follows: M. Termin for making the test samples, J. A. Sherrer for an analysis of the barium sulphate, and Miss V. P. Barton for photometering some of the plates.

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RADIATION REACTION OF METASTATIC SQUAMOUS CELL CARCINOMA IN CERVICAL LYMPH NODES*

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INTRODUCTION

RADIATION changes in normal and pathological tissues have been the subject of extensive historical studies, and sufficient data have been accumulated and recorded to render them a matter of common knowledge. Results of animal experiments with transplantable tumors as well as studies of irradiated tissues removed at operation have served as a basis for our present conceptions regarding the response of tissues to radiation. These familiar and well-known radiation effects have been observed daily in this laboratory. In spite of these extensive studies, no uniform nor constant relation between radiation and radiation effect has been determined, nor has it been possible to predict definitely what effect a certain type of radiation will produce.

In the course of routine examination of tissues in the laboratory a distinct change in the character and degree of radiation effect was observed. This change was particularly marked in cervical lymph nodes, the seat of metastatic squamous cell carcinoma. A superficial investigation revealed the significant fact that the change in tissue reaction was coincident with the institution of a more intensive form of radiation than had heretofore been employed.

A marked resistance to radiation of metastatic squamous cell carcinoma is a well-established clinical and histological fact. Effects upon these tissues following exposure to small doses of radium and roentgen rays have been so limited that it has been found necessary in most cases to follow the radiation by complete surgical removal. Recent observations in the laboratory have revealed effects upon these very resistant tumor cells of a degree and character never observed before. It is the purpose of this paper to record and interpret these observations.

METHOD

The routine procedure in the treatment of metastatic nodes in the neck has consisted of preoperative surface irradiation followed by surgical removal and postoperative irradiation. The operative material obtained from the routine neck dissections has consisted, therefore, of nodes, the seat of metastatic squamous cell carcinoma, which have been exposed to various types and intensities of radiation. This material has been utilized for purposes of studying the relationship between various forms of radiation and radiation effects with the following special considerations:

(1) To determine the type of radiation that has been most effective in destroying a very resistant type of cell, namely, that found in squamous cell carcinoma.

(2) To study the reaction of the lymphoid tissue to varying types and intensities of radiation.

(3) To study the mode of action of radiation in causing tumor regression.

Owing to the variability of factors influencing the biological response of tissues to radiation, the more constant the conditions under which a comparative study is made, the more nearly accurate the deductions. Absolutely rigid conditions can be applied only by resorting to animal experiments. In the choice of cervical lymph nodes invaded by squamous cell carcinoma we are dealing with a set of factors under fairly constant conditions.

1. The tumor cell under consideration is in all cases either a squamous or transitional cell carcinoma, each type showing a fairly constant and definite response to radiation.

2. The lesion irradiated is in all instances metastatic. Microscopic study of the primary lesion which was available in nearly every instance served as a control, permitting of a comparison between the primary non-irradiated tumor cell (obtained at biopsy) and the metastatic tumor.

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3. The site of metastasis or tumor bed is constant throughout the series, namely, lymphoid tissue.

4. The location of the cervical nodes relative to their distance from the skin, varies only within narrow limits.

5. Cases in which surgical removal was done at different intervals following irradiation of nodes on both sides of the neck permitted a comparison of the effect of the time interval upon tumor regression under otherwise similar conditions.

The material upon which this study is based is composed of forty specimens of cervical lymph nodes removed at operation, following surface irradiation of varying types and intensities. Gross and microscopic examination of metastatic nodes exposed to varying types of radiation presented the opportunity to compare the radiation employed with the corresponding tissue reaction.

The distribution of the primary lesion which gave rise to the cervical metastases is shown in the following table:

	Cases
Carcinoma of tongue	16
Carcinoma of tonsil	5
Carcinoma of maxilla	5
Carcinoma of larynx	4
Carcinoma of floor of mouth	3
Carcinoma of mucosa of cheek	3
Carcinoma of alveolar ridge	2
Carcinoma of accessory nasal sinuses	1
Carcinoma of lip	1
Total	40

Surface irradiation has consisted in some cases of the use of roentgen rays, in others of gamma radiation from radium emanation. In most instances a combination of the two has been employed.

Filtered radium emanation has been applied by means of the "pack" or the "tray." Both these applicators have a filtration equivalent to 2 mm. of brass. The "pack" has an area of 8 × 12 cm. and is applied at a distance of 6 cm. The "tray" has an area of 4 × 5 cm. and is applied at a distance of 3 cm.

In the employment of roentgen rays, two types of radiation have been utilized: so-called "high voltage" and "low voltage." The factors for these are tabulated as follows:

	Voltage (Peak)	Filter	Target-skin Distance	Ma.	Time (Min.)
High voltage	200 kv.	0.5 mm. Cu 1.0 mm. Al	50 cm.	4	(*a*) 60 (*b*) 80
Low voltage..	140 kv.	5.0 mm. Al	40 cm.	5	25
Low voltage..	140 kv.	4.0 mm. Al	30 cm.	5	15

The term "intensive radiation" is used in this discussion to designate a combination of high voltage roentgen rays and radium radiation applied to each side of the neck. In the treatment of those cases in which the resistant type of tumor cell is found the general plan has been to irradiate each side of the neck with high voltage roentgen rays (60 to 80 min., approximately 85 per cent of an erythema dose) and the radium "pack" (10,000 mc-hr.; approximately 90 per cent of an erythema dose). The entire cycle is usually given within a period of four to ten days. The dosage and interval of application are varied in so far as possible, according to the pathology of the lesion and the general clinical setting.

CLASSIFICATION OF CASES

A study of the effect of radiation upon tumor regression confirmed the original observation that favorable response of metastatic squamous cell carcinoma occurs following intensive radiation, and is only slight following smaller doses. To this general rule, however, a number of apparent exceptions were noted, In some cases in which small doses of radiation were employed, the response was extremely marked, in fact several specimens in which practically no trace of tumor cells could be found fell in this group. It therefore became necessary to search for other factors which might account for this apparent discrepancy.

Our present knowledge of radiation effects does not permit of accurate deductions as to what type of changes in tumor tissue may be expected to follow a given type of radiation. The biological response of tissues to radiation depends upon numerous factors which vary under different conditions and frequently under similar conditions. A rigid histo-radiological classification is therefore impossible. It is well known that structural characteristics of the tumor cells are of the

greatest importance in determining the dosage required to produce the biological response to radiation. Bergonié and Tribondeau have shown that the more embryonal or undifferentiated the type of cell, the greater is its radiosusceptibility. Conversely, the more adult or specialized the cell, the greater is its radioresistance (law of Bergonié and Tribondeau).

Within the group of epitheliomas a wide range of variation in the histological structure of the individual tumor cells exists. The structure is usually that of adult acanthoma with abundant keratosis and pearl formation. Many epitheliomas, however, exhibit transitional epithelial characters with cylindrical or cuboidal cells free from keratosis (Ewing).

A study of the individual tumor cells in the material at our disposal revealed two distinct types: The more common type is the adult fully developed and resistant squamous cell carcinoma (Fig. 1). In the other and less frequent variety of tumor cell, the squamous cell characters are lacking, keratosis and pearl formation are absent, the cell exhibits transitional epithelial characters and is designated by the term "transitional cell" (Fig. 2). The transitional type of cell is distinctly more radiosensitive than the squamous cell type and responds to smaller doses of radiation. The mode of disappearance of the two types of cell is also quite different. Upon the basis of these differences in the histological structure of the individual tumor cells, the cases are divided into two groups as follows:

Group I. Squamous cell carcinoma—Radioresistant—30 cases
Group II. Transitional cell carcinoma—Radiosensitive—10 cases

FIG. 1. Photomicrograph showing adult, fully differentiated squamous cell carcinoma. The cells are of the large pavement variety containing a small nucleus and relatively abundant cytoplasm.

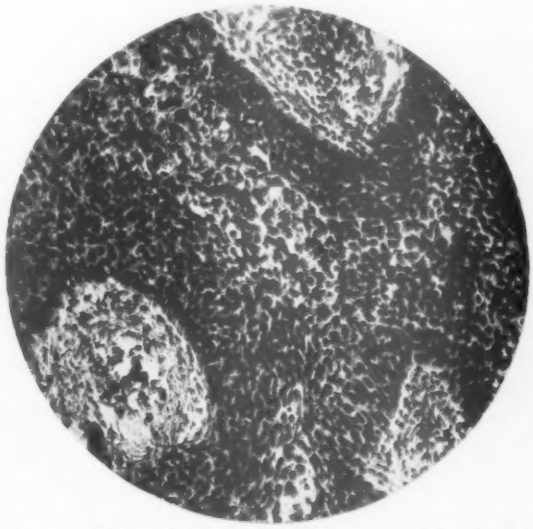

FIG. 2. Photomicrograph showing transitional cell carcinoma. The cells are small, the nuclei hyperchromatic, squamous characters are lacking. The cell is made up almost entirely of nucleus. There is very little intercellular substance.

CLINICAL ASPECTS

The clinical aspects of each case are considered only in so far as they may have a bearing upon the biological reaction of the tissue to radiation. In the course of analysis of the clinical data, certain clinical features were noted to have a particularly important bearing upon tumor regression. The age of the patient, his general physical condition, the duration and condition of the lesion when radiation was first employed, are all important factors influencing tissue reaction.

Of particular importance is the presence of infection in tissues exposed to radiation. Instances in which the nodes had been incised, either in an attempt at partial removal or at biopsy, responded very

poorly to radiation. The stimulating effect of infection upon tumor growth and the unfavorable radiation regression of infected tumors are well established clinical facts. To this is added histological proof of the lack of response of tumor cells to radiation in the presence of infection. In several instances in which apparently adequate radiation resulted in poor regression extensive infection was noted, and further investigation revealed a history of recent incision.

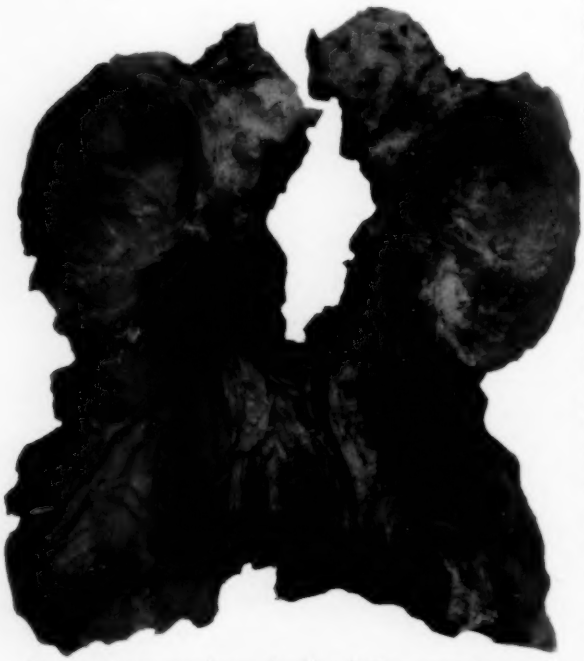

FIG. 3. Gross specimen showing bulky central necrosis and cystic degeneration of lymph node following radiation. The capsule is intact, fibrosed, the remaining tissue is composed of necrotic degenerated tumor cells.

GROUP I. SQUAMOUS CELL CARCINOMA

Discussion. In this group are included those cases in which the tumor is composed of cells showing fully developed squamous cell characters. The stubborn resistance of these cells to surface radiation has long been recognized. The occasional unexpected result following small doses has upon more detailed investigation frequently revealed that the type of cell has belonged to the transitional and not the squamous cell group. Small doses of radiation have been found to exert only slight effects upon the resistant type of cell. On the other hand, marked destructive effects have been observed following intensive irradiation. Those nodes which have been treated with combined high voltage roentgen rays and radium have shown particularly marked regression.

Gross Pathology. Gross examination of the nodes reveals distinct and uniformly characteristic anatomical changes. A description of these changes as radiation effects is given with due recognition of changes encountered in carcinomatous nodes undergoing spontaneous degeneration. Many of the features described are undoubtedly the combined result of a spontaneous degenerative process and radiation effect.

One of the most striking features observed by gross examination of nodes which have been heavily irradiated is a marked thickening and fibrosis of the capsule. The degree of fibrosis varies with the amount of radiation employed. The fibrosis of the capsule acts as an effective barrier to further invasion by tumor growth. In only four instances has the tumor perforated the gland capsule and invaded muscle tissue. The submaxillary salivary gland, removed along the lymph nodes in the course of submaxillary dissections has been invaded by tumor in only one instance.

The encapsulation of the nodes in a firm fibrotic capsule is of distinct value. By confining the tumor growth within the capsule of the node, the rate and degree of extension are limited and tumor regression is favored. An outstanding clinical improvement based upon this radiation effect has been the prevention of broken down, ulcerating and discharging tumors in the neck due to perforation of the capsule followed by secondary infection.

Another fairly constant and uniform change observed by gross examination of the specimens is the massive central necrosis. The degree of necrosis varies, the more heavily irradiated nodes showing distinctly a more marked effect. As can be seen from the photographs, many of the specimens show complete destruction of the center of the node surrounded by a shell of devitalized tumor tissue enclosed

in a thickened capsule (Figs. 3 and 4). This effect is undoubtedly of vascular origin and must be regarded as an anemic necrosis. The bulky necrosis of the center of the node seen in these cases is in most instances probably the result of spontaneous degeneration with a superimposed radiation effect. In several specimens the destruction has been so complete that the entire node is seen to be replaced by loose friable necrotic material enclosed in the gland capsule. No gross nor microscopic evidence of tumor tissue can be demonstrated.

FIG. 4. Gross specimen (J. S.) after radiation. Primary lesion was carcinoma of tonsil, transitional cell type. Microscopic examination showed complete tumor destruction (see Figs. 9 and 10).

Histological Changes. An outstanding feature of the histological changes observed in those cases in which a favorable radiation effect has occurred, has been the extremely favorable reaction of the tissues adjacent to the tumor. Marked regression of the tumor has been accompanied by a most favorable tumor bed reaction. This has consisted of an active proliferation of the connective tissue, proliferation of young fibroblasts, exudation of lymphocytes, leucocytes and plasma cells, upgrowth of new capillaries, and formation of granulation tissue (Fig. 5).

Associated with this reaction in the tissues adjacent to the tumor, marked changes within the tumor itself are observed (Fig. 6). The tumor mass is broken up by the invading connective tissue, first, into smaller fragments, then into cell groups, finally into isolated tumor cells. These become surrounded by and incarcerated in the actively growing connective tissue stroma. The centers of the cell groups then become the seat of active phagocytosis and begin to undergo liquefaction necrosis. In the meantime the individual tumor cells are undergoing a series of degenerative changes, consisting of swelling of the cytoplasm, hydropic degeneration of the cell bodies, hornification, calcification, cell atrophy and complete necrosis.

The favorable response of the tissues adjacent to the tumor described above is absent following smaller doses of radiation. In response to smaller doses the center of the node usually shows the most marked changes, hornification, calcification, and central necrosis are the outstanding features, the adjacent tissues are only slightly altered. Activity of the connective tissue such as occurs following intensive irradiation is slight or altogether absent. The cellular reaction is not marked. The histological picture shows all the characteristic features of a central necrosis, differing in this respect from the type

of reaction following combined and intensive roentgen-ray and radium therapy. In the latter group the tissue architecture is altered, the radiation appears to affect primarily, the connective tissue, plasma cells and lymphocytes, and secondarily the tumor cells (Figs. 7 and 8).

FIG. 5. Photomicrograph showing extremely favorable tumor bed reaction. There is marked exudation of plasma cells and lymphocytes, active proliferation of the connective tissue, isolated islands of tumor cells are undergoing degenerative changes.

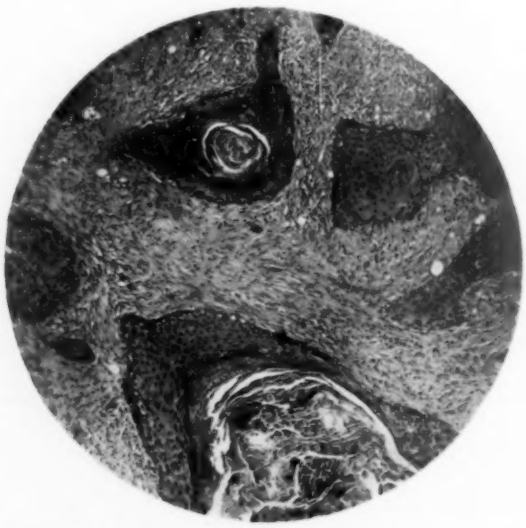

FIG. 6. Photomicrograph showing groups of tumor cells beginning to show central hornification. (Squamous cell carcinoma.)

FIG. 7. Photomicrograph showing islands of squamous cell carcinoma showing hornification. Note the groups of leucocytes in center of cell masses with beginning phagocytosis and central liquefaction necrosis.

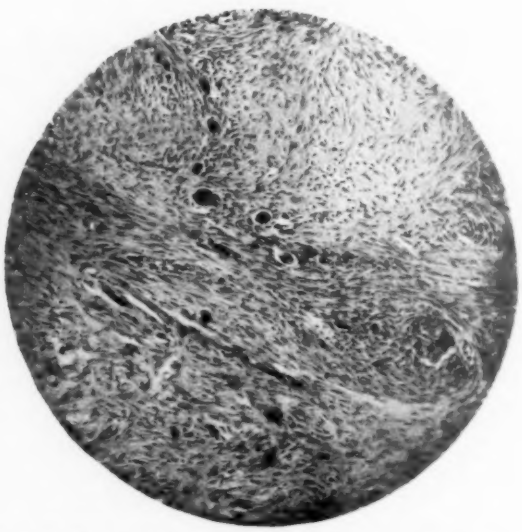

FIG. 8. Photomicrograph showing active proliferation of the connective tissue. Groups of tumor cells have been broken up into single tumor cells some of which are already beginning to show loss of cell outline.

GROUP II. TRANSITIONAL CELL CARCINOMA

Discussion. The variation in the clinical course of tonsillar, lingual and laryngeal carcinomas has been commonly observed. Some of these tumors progress rapidly, metastasize early, and are subject to ulceration and early suppuration; others

grow more slowly, tend to remain localized for a longer period of time and metastasize late. The clinical course is undoubtedly much influenced by the type and location of the tumor (Ewing).

The phenomenal disappearance of certain tumors following small doses of radiation is a well-known clinical and histological observation. Of all the factors which influence the biological response of a tumor cell to radiation, the degree of differentiation of the cell is one of the most important. It has been noted that the most marked effects have frequently occurred in response to radiation of a type ordinarily inadequate in destroying the resistant squamous cell carcinoma. A study of the character of the tumor cell as seen in the nodes, confirmed by observation of the type of cell as seen in the primary lesion demonstrates that in most of these cases the tumor cell has been of the transitional and not the squamous cell variety (Figs. 9 and 10).

In this group are included those cases in which the tumor is made up of the transitional type of cell. The regression of the primary lesion and cervical nodes following radiation, as well as the subsequent clinical course of these cases has been particularly favorable. It is noteworthy that in 5 of the 10 cases in this group the lesion has been located in the tonsil.

Gross and Histological Changes. The gross changes observed in the specimens in this group of cases are similar to those observed in Group 1, of which a detailed description has been presented.

The histological picture is different and is quite characteristic. The mode of regression of the tumor is very different from the response to radiation of the more resistant type of cell. Massive liquefaction necrosis is the outstanding feature, the cells become small and shrunken, the nuclei pycnotic, there is massive destruction of tumor tissue, leaving only shadows of cells with occasional nuclear fragments scattered in the field; hornification, calcification and fibrosis are absent, the tumor cells apparently disappear too rapidly for these processes to occur. The reaction of the tissues adjacent to the tumor is marked by a rich exudation of lymphocytes and plasma cells, accompanied by proliferation of fibroblasts and formation of granulation tissue.

It is interesting to note that these effects upon tumor regression, as well as the favorable tumor bed reaction in this group of cases, have been obtained follow-

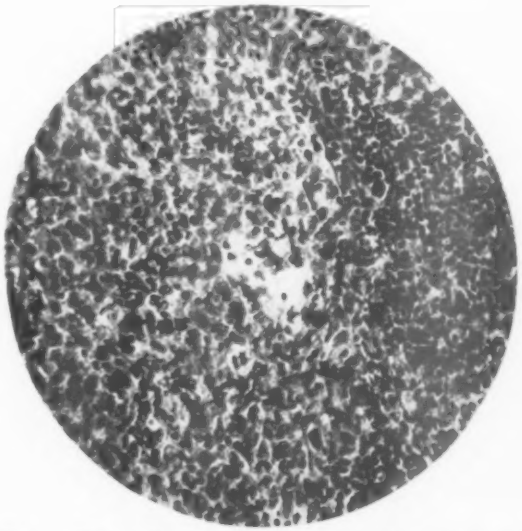

FIG. 9. Photomicrograph of biopsy specimen from primary lesion of transitional cell carcinoma of tonsil. Note the mitotic figures.

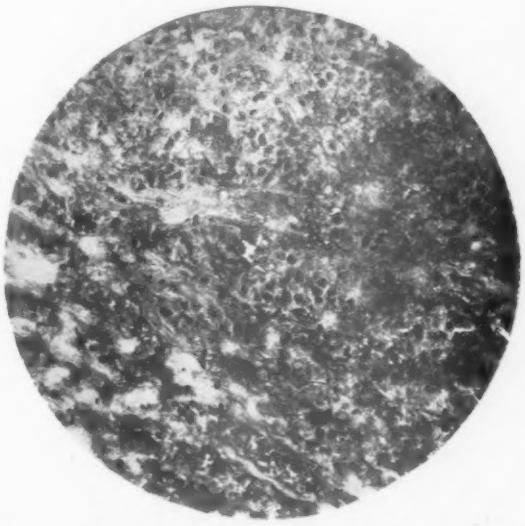

FIG. 10. Photomicrograph of metastatic lymph node from same case after irradiation. There is complete destruction of tumor tissue; the darkly stained nuclei are remaining lymphocytes. (Fig. 4 shows the gross specimen from this case.)

ing small doses of radiation. These tumors evidently require radiation of a smaller intensity to cause their destruction.

Lymphoid Tissue Reaction. During the course of our observations on the effects of radiation upon squamous cell carcinoma in lymph nodes, an unusual opportunity presented itself to study and observe the effects of radiation upon the lymphoid tissue in the nodes invaded by carcinoma as well as in lymph nodes free from metastatic invasion. The outstanding feature of these observations is that in spite of the large dosages employed, the lymphoid

FIG. 11. Photomicrograph showing hyperplasia of the lymphoid tissue following intensive irradiation. The lymph follicles are edematous, the endothelial cells are prominent, and the germinal centers contain numerous mitotic figures.

tissue is resistant, and adjacent uninvolved nodes instead of becoming atrophic, become enlarged and show definite evidence of hyperplasia. The sudden appearance of lymph nodes during or following radiation therapy is a common clinical observation. The proper interpretation of this phenomenon is of practical importance. This occurrence may be ascribed to one of several causes: In a certain number of these cases, the sudden enlargement of these nodes may be due to the presence of infection in the primary focus. The effect of radiation upon tissues, the seat of an inflammatory process, may in certain instances account for the appearance of these nodes. Frequently, however, these nodes have suddenly appeared in cases in which this factor may be reasonably excluded. Histological examination of such nodes removed during neck dissections has revealed a marked lymphoid hyperplasia. Frequently, during the course of ligation of vessels of the neck following irradiation, such nodes have been encountered and removed. Examination of these has also shown the same histological picture. The enlargement of the lymph nodes under discussion is quite distinct from the enlargement of nodes due to inflammatory irradiation. The latter process soon subsides and the nodes usually return to their original size. This peculiar hyperplasia of lymph nodes has been especially marked following intensive irradiation.

The histological picture observed in these cases is very striking. The lymphoid tissue is resistant, the lymphocytes retain their cell outline, the nuclei show light striations but retain their form. No karyolysis nor karyorrhexis is evident. The lymphoid follicles stand out prominently and appear enlarged and edematous. The germinal centers contain numerous mitotic figures; the endothelial cells appear normal. In some instances extensive interstitial miliary hemorrhages are encountered; occasional eosinophiles are seen (Figs. 11 and 12).

The first systematic attempt to study the nature of the changes set up in the internal organs of animals subjected to roentgen rays was made by Heineke, who in 1905 published the details of his investigations of studies made upon guinea pigs, rabbits and dogs. He observed that following exposure to radiation, changes occurred in lymph nodes, consisting of a destruction of a greater part of the lymphocytes in and around the follicles. He states that the effect of radiation is the destruction of lymphoid tissue in every region of the body. The rapidity with which these changes occur render it most probable that the effect is a direct one and that of all cells the lymphocyte is among the most vulnerable to roentgen rays. These observations were later confirmed by Menetrier and Touraine. Murphy and

his coworkers at the Rockefeller Institute have shown, also in animals, that by properly regulated small doses of roentgen rays it is possible to produce a marked stimulation of the lymphoid organs, and a lymphocytosis in the circulating blood. The presence of a stimulating effect was judged by the number of circulating lymphocytes and the state of activity of the germinal centers by the number of mitotic figures present. Within four days after exposure of mice to roentgen rays there appeared an abnormally large number of mitotic figures in the lymphoid tissue, indicating an acceleration of the proliferative activity of the lymphocytes.

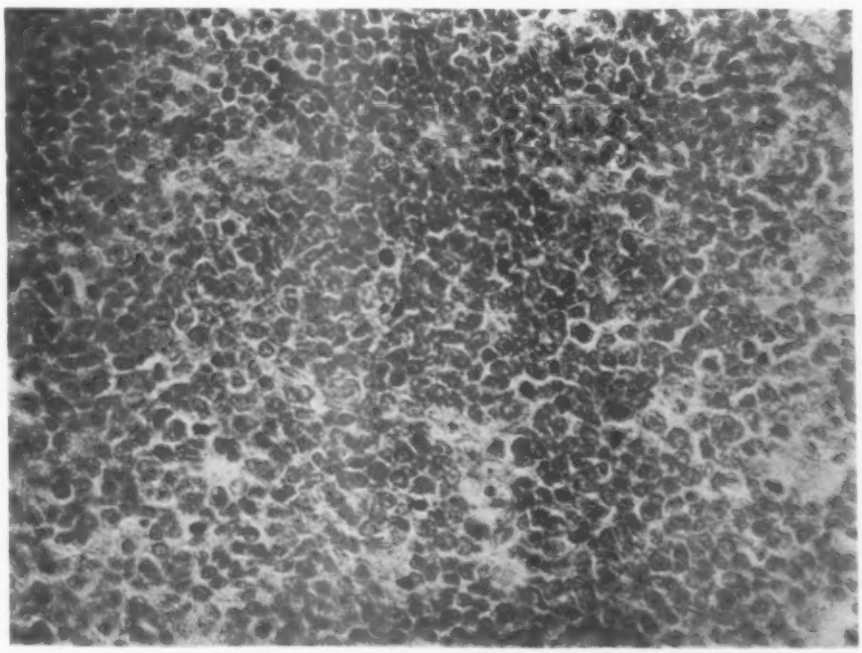

FIG. 12. Photomicrograph showing numerous mitoses in germinal center of cervical lymph node following intensive surface irradiation (combination high voltage roentgen rays and radium).

Normal lymphoid tissue has been found to resist large doses of radiation. Ewing has made this observation repeatedly. In a number of specimens he has pointed out the presence of numerous mitotic figures in the germinal centers, showing an active proliferation of the lymphoid elements in nodes which have been heavily irradiated. The significance of this peculiar reaction of the lymphoid structure to radiation is difficult to interpret. Whether it is indicative of a state of heightened resistance against invasion by tumor growth awaits further observations along this line.

THE MODE OF ACTION OF RADIATION UPON CARCINOMA

The histological observations included in this study demonstrate that favorable radiation regression of tumor cells occurs most commonly in the presence of a favorable reaction in the surrounding tissues. The constant association of a favorable tumor bed reaction with tumor regression and the poor radiation effect upon tumor cells surrounded by tissues in which this reaction is missing, strongly suggest that the mode of action of radiation is an indirect one. It is furthermore not unlikely that the marked connective tissue and cellular responses are an expression of a general reaction on the part of the entire organism rather than a local radiation effect.

Ewing has repeatedly emphasized the significance of the reaction of the tissues adjacent to the tumor in causing tumor regression. It is upon the state of

these tissue elements that the result of radiation will largely depend.

The mode of disappearance of the transitional type of cell is extremely

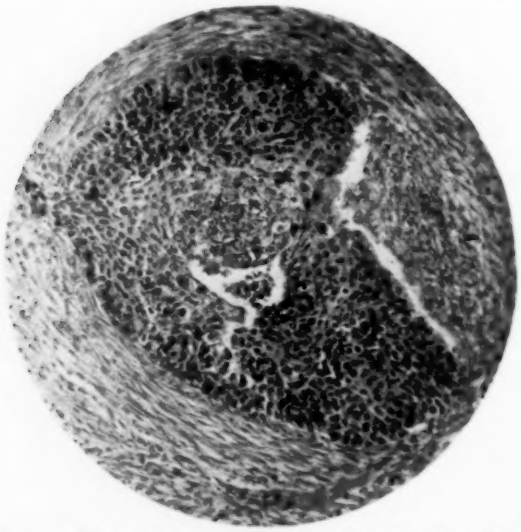

FIG. 13. Photomicrograph showing the typical mode of disappearance of transitional cell carcinoma. A group of tumor cells is surrounded by connective tissues beginning to show central liquefaction necrosis.

interesting and furnishes a wide field for speculation. The presence of a marked cellular exudation and a favorable con-

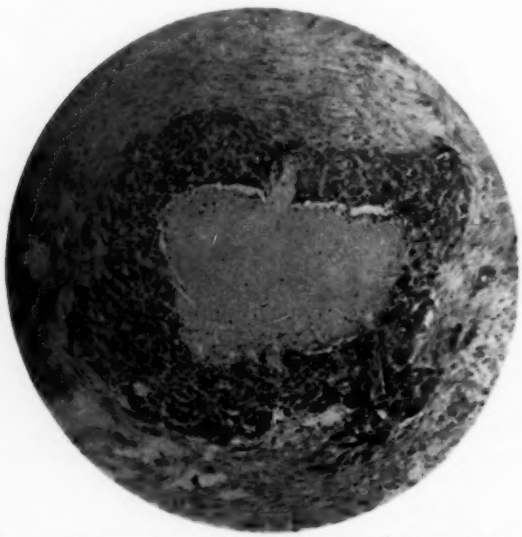

FIG. 14. Photomicrograph showing stage of liquefaction necrosis.

nective tissue reaction in response to small doses suggest some relationship between the favorable tumor bed reaction and the rapidly disappearing tumor cell. The rapid liquefaction necrosis has been attributed by some to the action of an autolytic ferment. The production of such an agent would account for the marked cellular reaction associated with the disappearance of this type of tumor (Figs. 13 and 14).

A close study of the histological material included in this presentation demonstrates that relatively large amounts of radiation may be introduced into tumor tissue without injuring the surrounding normal structures, and that it is possible to deliver

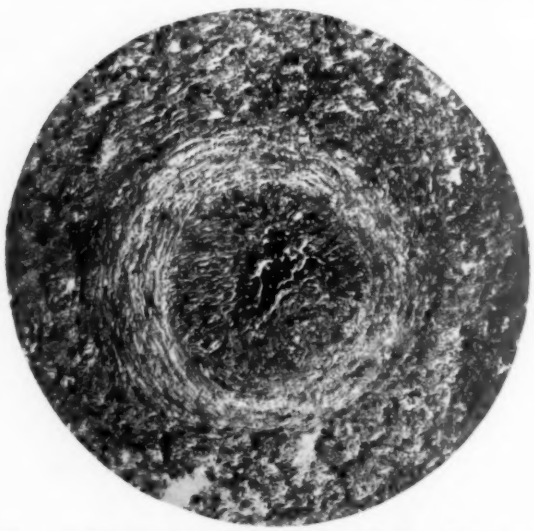

FIG. 15. Photomicrograph showing radiation effect upon small blood vessel. Note thickening of vessel wall, almost complete occlusion of the lumen and the perivascular lymphocytic infiltration.

to the tumor an optimum dose of radiation which will cause effective regression of tumor cells and at the same time not injure but stimulate the surrounding connective tissue and cellular elements.

SUMMARY AND CONCLUSIONS

1. The purpose of this work was (*a*) to study the effects of various types and intensities of radiation upon metastatic squamous cell carcinoma in lymph nodes; (*b*) to study the mode of action of radiation in causing tumor regression, and (*c*) to study the reaction of the lymphoid tissue to varying types and intensities of radiation.

2. The material upon which this study is based was composed of 40 specimens of

cervical lymph nodes, invaded by squamous cell carcinoma, which have been removed following surface irradiation.

3. A study of the character of the individual tumor cells revealed two distinct types: The adult fully differentiated squamous cell, and a transitional type of cell in which squamous characters are lacking. The former is radioresistant and its response to radiation depends upon the type and intensity of radiation employed. The latter is radiosensitive and responds favorably to smaller doses. Based upon these histological characteristics, a division of the cases into two groups was made.

4. Marked destructive effects upon squamous cell carcinoma were obtained by means of intensive irradiation with combined high voltage roentgen rays and radium. Small doses of roentgen rays or radium alone, or in combination, were wholly inadequate in their effects upon the resistant type of tumor cell.

5. Small doses of radiation which had little or no effect upon the squamous cell were found to cause rapid and effective regression of the transitional type of tumor cell.

6. Gross pathological changes in the nodes have consisted of fibrosis and thickening of the capsule and a central necrosis.

7. Three distinct types of radiation regression were observed:

(*a*) Massive central necrosis accompanied by little or no reaction in the adjacent tissues, the central necrosis may be due largely to spontaneous degeneration of the tumor.

(*b*) A histological picture in which the favorable reaction in the tissues adjacent to the tumor is the outstanding feature, (connective tissue stimulation, and rich plasma cell and lymphocytic exudation) in which the radiation effect is diffuse and uniform throughout the tissues, and in which effective regression of the tumor is observed. This is the type of reaction associated with combined, intensive roentgen-ray and radium radiation.

(*c*) Rapid and massive liquefaction necrosis associated with a rich exudation of lymphocytes and plasma cells following radiation of the transitional type of tumor cell.

8. It was found that radiation regression of the tumor was most effective when associated with a favorable reaction in the adjacent tissues, and least effective when this reaction was missing.

9. Intensive radiation with repeated high voltage roentgen rays and radium has not injured the tissues adjacent to the tumor; on the contrary, a stimulating effect upon the tumor bed has been frequently observed.

10. Normal lymphoid tissue was observed to resist large doses of radiation. A peculiar lymphoid hyperplasia occurs, the nodes become enlarged, the lymph follicles prominent and the germinal centers contain numerous mitotic figures.

The writers wish to acknowledge their indebtedness to Dr. James Ewing for his invaluable aid throughout this entire study.

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DISCUSSION

Dr. James Ewing, New York City. There are two points that might be mentioned regarding the changes in the lymph nodes which Drs. Quick and Cutler have shown. Some of these

changes may be regarded as occurring in the natural course of epidermoid carcinoma in the cervical lymph nodes. These metastatic tumors sometimes undergo cystic degeneration, and the tumor may be reduced to a thin rim of tissue beneath a thickened capsule of the node. It is not always easy to pick out just which of the changes seen in irradiated lymph nodes are due to the radiation. Yet from a study of many nodes I feel reasonably sure that the extensive hornification, necrosis, cell reaction, and fibrosis are true radiation effects, which are not seen in such degree in the natural course of squamous cell carcinoma in the lymph nodes.

The existence of two quite different types of epidermoid carcinoma, from the radiation standpoint, have been demonstrated by Drs. Quick and Cutler, in these nodes. One is the ordinary adult squamous hornifying carcinoma, which is very resistant to radiation. The other may be called the transitional cell type, since the cells do not become squamous and do not produce horny material. The latter type does not arise from the squamous lining of the lip, tongue, or buccal surface, but apparently from the tonsil, posterior nares, and vault of the pharynx, and possibly from deeper structures in the submucosa, such as gland ducts. They are very much more susceptible to radiation than the squamous type.

The danger of late sequelae from very heavy radiation of the neck must be considered. We do not know what may happen a year or so after such treatment, but as Dr. Quick has said to me, we know what will happen if we don't give this vigorous radiation to these infected nodes.

Dr. H. K. Pancoast, Philadelphia. The explanation offered by Dr. Cutler and Dr. Ewing for some of the remarkable results we sometimes observe in the treatment of advanced mouth cases in attributing these results to the transitional cell type of carcinoma, which is unusually susceptible to irradiation, is a most interesting one. It explains why some of our apparently hopeless mouth cases have miraculously improved or gotten well. It is especially gratifying to know that this cell type may sometimes be found in the deeper carcinomas of the tongue, which we have occasionally observed to improve under external deep roentgen therapy alone, when used as a palliative measure. The explanation is also satisfactory for the more favorable action of irradiation upon tonsillar carcinoma, including metastatic glands in the neck.

Dr. George E. Pfahler, Philadelphia. I would like to confirm what Dr. Pancoast has just said, which explains a group of cases which we meet. I would like to emphasize what Dr. Ewing and Dr. Quick have said; that we are likely to run into damaging effects from this heavy radiation, but since it is the only thing that we can do for these patients with our present knowledge, it behooves us to explain to the family and friends that some damaging effects may occur. We must also explain what Dr. Ewing has said,—that we know what will happen if the treatment is not given. It may be well to have the patients or friends sign a statement that they have had fully explained to them the dangers that may occur.

Only yesterday one of the doctors told me that he had cured a carcinoma of the tongue, which required heavy radiation, and now, although the patient is apparently entirely well, he is turning around and suing one of our members because of what he calls a "radium burn." Naturally, it required a very serious damaging effect to that tongue in order to get the case well; but that is the sort of thing we are going to meet.

Dr. Quick, closing. Just one thing that has been rather suggested to us; last year, I don't know whether it was in a communication before this Society or before one of the other societies, Dr. Wood presented some work which indicated that differences in wave length had nothing to do with the effects on tissues. It has seemed to us that there has been some difference. From clinical observation, it seemed to me so, and microscopically, Dr. Cutler and Dr. Ewing have been inclined to agree that radium apparently has a more marked influence on the cellular elements, whereas radiation perhaps has a bit more marked influence on the connective tissue, on the production of new connective tissue. Of course, the only difference which we apparently recognize between the two agents is the difference in wave length, and I wonder after all if there isn't a definite clinical difference, a different response to radiation, depending upon the wave length.

RADIOTHERAPY IN INOPERABLE CARCINOMA OF THE CERVIX*

BY CLARK D. BROOKS, M.D.

DETROIT, MICHIGAN

CANCER of the cervix makes up 80 per cent of the cases of cancer of the uterus. The cervical cancers are of two varieties: the epithelial type or squamous cell carcinoma, involving the vaginal mucous membrane of the cervix, and adenocarcinoma, which begins in the columnar epithelium of the cervical canal. The squamous cell variety is about four times as common as adenocarcinoma, and it is relatively more malignant.

The malignancy of cancer of the cervix varies as in cancer elsewhere; the higher grades of malignancy being found in young patients. Some cases metastasize relatively early, other cases are checked by low pelvic lymphatics. Some cases may metastasize to the liver before there is any marked metastasis in the pelvis.

Lymphatics. According to Poirier and Cuneo, the cervix has three sets of lymphatics. The first passes outward and upward along the side of the pelvis anterior to the ureter to empty into the nodes along the external iliac artery. The second set passes backward behind the ureter to empty into a node on the anterior division of the internal iliac artery. The third set passes from the posterior surface of the cervix almost directly backward in the uterosacral ligaments to empty, some into the lateral sacral nodes high up in the hollow of the sacrum and some into the nodes of the promontory.

Operability. It is difficult to classify operable. What may be considered inoperable at one clinic may be considered operable in another. This condition may also vary with the skill of the surgeon, and whether or not he is familiar with and has available the use of radium or deep roentgen therapy, or is familiar with and has available the use of the cautery, especially the cooled speculae and cautery of Percy. We wish however to classify the cases in this series as inoperable when they have presented one or more of the following symptoms or manifestations: (*a*) Severe sacral pain; (*b*) when the cancer has extended from the cervical vaginal mucosa to the vaginal mucosa; (*c*) fixation of the uterus in the *cul de sac;* (*d*) involvement of the rectum; (*e*) marked cachexia, and (*f*) known metastasis.

A certain number of inoperable cases may become operable after the use of radium, cautery or roentgen therapy. We believe that the best method in these cases is to use from 50 to 100 mg. of radium in a Universal applicator in the cervical canal, when the cervical canal has not been destroyed, or in the form of needles, properly spaced, when the cervical canal has been destroyed, and at times using needles with radium in the cervical canal. The average treatment has been from 2400 to 4000 mg-hr. Formerly, we treated some of our patients with radium in this manner, and repeated at intervals of three weeks. In the last three years, however, we have thought that the best method is to use radium as above, and repeat in three days, with perhaps a third treatment, all of which should be given within the first ten days, followed immediately by deep roentgen therapy, when the patients are in a condition for this. If we think they cannot stand severe radiation sickness we give them large doses of alkalies, forced fluids and food, saline and glucose by enteroclysis, glucose intravenously and, if necessary, blood transfusions, and then follow with deep roentgen therapy as soon as the patient's condition will warrant it.

In our series of cases, there has been none on whom we have advised radical operations after the above routine treatment, even when the disease has apparently been arrested within three months after treatment.

We believe the danger of vesicovaginal fistulas and rectovaginal fistulas will be lessened by the method of intensive radium

* Read at the Tenth Annual Meeting, AMERICAN RADIUM SOCIETY, Atlantic City, N. J., May 25–26, 1925.

treatment given within a week or ten days from the time of the first treatment.

We have had 2 cases of vesicovaginal fistula in our entire series. Each occurred within four months from the time of radium treatment but neither until after three months. Cases occurring after four months we do not believe should be considered as caused by radium reaction.

We have not practised biopsy, that is, by the use of the curette, in any of our cases, but find that if the case is far enough advanced a section can be rubbed off with a gentle application of gauze on a tissue forceps. We consider that the curette in cases of this type is contraindicated and dangerous, and should not be used when it is possible to obtain a specimen or make a diagnosis without it. If it is necessary to use a curette to obtain a section for diagnosis, we consider immediate use of the cautery and radium to be imperative.

We always consider that radium treatment with or without deep roentgen therapy is a major operation and protect our patients in every possible way—by strict asepsis, administering a gas anesthetic, if an anesthetic is used, and forced fluids, followed by alkalies and alkaline douches, with supportive treatment.

All the patients who have received deep roentgen therapy have received it in the roentgen department of Harper Hospital under the direction of Dr. Wm. A. Evans and his associate, Dr. T. Leucutia.

RESUMÉ OF 100 CASES OF INOPERABLE CARCINOMA OF THE CERVIX

Multipara	89	Nullipara	11
Cases under 35 years of age			8
Cases between 35 and 45 years of age			24
Cases between 45 and 55 years of age			48
Cases over 55 years of age			20
Average duration of symptoms when first consulted			9 months
Patients who received 1 intensive radium treatment			72
Patients who received 2 radium treatments			21
Patients who received 3 or more radium treatments			7
Patients who received deep roentgen-ray treatments with radium treatments (since 1922)			26
Patients clinically well after 1 year			18
Patients clinically well after 2 years			11
Patients clinically well after 3 years			3

EVALUATION OF TREATMENT OF CARCINOMA OF THE CERVIX WITH RADIUM*

BY WILLIAM P. HEALY, M.D., F.A.C.S.

NEW YORK CITY

IN the years that have elapsed since radium has been available for the treatment of carcinoma much effort has been expended by different groups of workers in developing the field of radiation therapy. Despite individual differences of opinion regarding methods of procedure, the use of a massive dose of radiation or of repeated small doses, of combining roentgen rays with radium, or one or both with surgery, there has come about a unanimity of opinion regarding the advantage of radiation therapy in so far as carcinoma of the cervix is concerned. This has resulted largely from the work of Janeway, Bailey, Schmitz, and J. G. Clark in this country, and of Regaud, Forssell, Heyman, and others in Europe. During this time we have learned much regarding the effects of radiation therapy on the tissues and the reaction of the tissues to doses of varying intensity through the splendid studies of Ewing on the tissues removed by hysterectomy after irradiation.

We know that with radiation therapy properly applied, in so far as radium is concerned, we can with a reasonable degree of certainty expect a definite sequence of reactions in the tissues treated and the adjoining structures. These changes consist in a gradual disintegration and disappearance of the cancer cells in one to three weeks and the appearance in the tissues of lymphocytes, polymorphonuclear leucocytes and plasma cells in large numbers. Finally, a replacement

* Read at the Tenth Annual Meeting, AMERICAN RADIUM SOCIETY, Atlantic City, N. J., May 25–26, 1925.

fibrosis occurs varying, we believe, in degree with the extent of the original neoplastic disease. We have also been impressed with the difference in the constitutional or systemic reactions of individual patients to radiation therapy. Following out as we do at the Memorial Hospital a fairly well standardized technique, we nevertheless find tremendous variations in the constitutional reactions of the different patients. Some show marked gastric symptoms with mental depression from the beginning of treatment, with gradually increasing toxic symptoms for two to four or more weeks after treatment. Others show practically no radiation sickness or systemic intoxication beyond a feeling of malaise and lack of energy for several weeks after treatment. In fact, we are inclined to believe that these constitutional symptoms are often more marked in the younger women, especially those of a nervous temperament, and are largely dependent upon an endocrine imbalance resulting from the treatment. For that reason we promptly institute oral and hypodermic medication to combat these symptoms.

Nor, on the other hand, have we found any definite connection between the extent of the primary lesion and the degree of intoxication following the treatment. In general, we find that it takes about six weeks for patients to begin to recuperate after the treatment as carried out by us.

The general plan of treatment is that instituted by Bailey in 1917 and depends upon the principle of cross firing the lesion and the entire pelvic field with radium applied in capsules, within the uterine cavity, in "seeds" in the lesion, in the bomb *per vaginam*, and with low voltage roentgen rays externally. Previous to 1922 the external treatment was given with small radium packs. This was not found to be as satisfactory from the practical standpoint, as it required the use of too much radium, nor as efficient from the standpoint of intensity of percentage depth dose as the roentgen ray. For that reason we have used roentgen rays for external irradiation since January, 1922. The total dosage of radium applied in and about the lesion exclusive of the external radiation is between 6000 and 9000 mc-hr.

From a review of the reports of the investigators named in the forepart of this paper and a study of our own cases we believe that radium today is the best single therapeutic agent in the control of uterine cervical cancer; that it is of greater value in the care of all the cases that apply for treatment than any other form of therapy and that its usefulness is not restricted to any one group of cases but is indicated in every case which is not hopelessly advanced or complicated by extensive pelvic infection.

It is now a matter of common experience that radium applied at the site of the primary lesion will in all but the most advanced cases cause a rapid regression and disappearance of the lesion in ten days to three weeks. Many of these patients have then been subjected to panhysterectomy and a careful microscopic study of the tissues removed has frequently failed to reveal any evidence of cancer, thus corroborating the clinical evidence that the disease had been eradicated.

With this evidence in hand, it is difficult to understand why these patients should any longer be subjected to a dangerous surgical procedure for the removal of an organ which has been purged of its disease by previous irradiation. If the irradiation has been effectively carried out the subsequent operation is unnecessary and may be harmful, whereas if the irradiation has been ineffectively instituted then the operation is useless, as experience has shown, for the cancer rapidly recurs in the parametrium.

We know of no statistics indicating that preoperative irradiation of the lesion with subsequent hysterectomy has any advantage over irradiation alone when properly carried out, and we believe that there are sound theoretical considerations for believing that this combination of irradiation followed by operation may seriously handicap the patient from obtaining the full benefit of either procedure. It seems reasonable to assume that the orderly protective reaction in the tissues set up by the radiation therapy will be largely if not entirely interrupted by the surgical procedure because of interference with the norma

blood supply to the tissues. Moreover, the tendency on the part of surgeons using preoperative radiation therapy is to do a simple panhysterectomy instead of a radical Wertheim operation, thus depriving the patient of the benefit of the best surgical procedure for the treatment of cancer of the uterine cervix. Thus it would seem that these patients have had neither good irradiation nor good surgery and that the plan should be dropped. Based upon our statistics it would seem much more justifiable to do an immediate hysterectomy in the very favorable case and follow the operation promptly with thorough cross fire irradiation of the pelvic field with radium and roentgen rays.

During the past ten years, that is from January, 1915 to December, 1924, inclusive, 1173 cases of cancer of the uterine cervix have been admitted to the gynecologic service of the Memorial Hospital for radiation therapy.

In the earlier years no definite plan of treatment had been instituted, but in 1917 Harold Bailey established the cross fire principle and developed the technique, using radium for the entire procedure.

TABLE I

CASES TREATED BY RADIUM THERAPY

1918 to 1921 Inclusive

(Service of Dr. Harold Bailey)

	Total	Alive Jan. 1, 1925	Alive, Per Cent
Cervix			
Early	35	14	40
Borderline	52	14	27
Advanced	288	25	8.6
Total cervix	375	53	14
Recurrent cervix	139	28	20
Postoperative irradiation	25	16	64

Since that time this technique has been followed, with the important exception of changing to the use of low voltage roentgen therapy for external irradiation in 1922.

Tables I, II, and III show in statistical form the results of treatment from 1918 to 1924 inclusive.

TABLE II

CASES TREATED BY COMBINED RADIUM AND ROENTGEN THERAPY

1922 to 1924 Inclusive

(Service of Dr. William P. Healy)

	Total	Alive	Alive, Per Cent
Cervix			
Early	44	41	93
Borderline	57	42	73.6
Advanced	252	113	44.8
Total cervix	353	196	61
Recurrent cervix	71	41	57.7
Postoperative irradiation	5	5	100

TABLE III

	Advanced Cervix	Borderline Cervix	Early Cervix	Recurrent Cervix	Prophylactic
1918	41 (4)	17 (3)	4 (0)	35 (4)	8 (3)
1919	69 (3)	10 (0)	8 (4)	43 (5)	4 (3)
1920	92 (6)	12 (3)	13 (3)	37 (14)	10 (7)
1921	86 (12)	13 (8)	10 (7)	24 (5)	3 (3)
1922	80 (20)	27 (12)	16 (14)	29 (11)	2 (2)
1923	81 (28)	8 (8)	12 (12)	24 (12)	1 (1)
1924	91 (65)	22 (22)	16 (15)	18 (18)	2 (2)

Numbers in parenthesis indicate patients alive Jan. 1, 1925.

CONCLUSIONS

1. From a study of our statistics it would seem reasonable to assume that a diagnosis of cancer of the uterine cervix is an indication for radium therapy.

2. Operation is justifiable only when serious contraindications to radiation therapy are present.

DISCUSSION ON PAPERS OF DR. BROOKS AND DR. HEALY

DR. HENRY SCHMITZ, Chicago. In discussing a symposium of this kind it is impossible to dwell on all the points. I will take up first the classification of cases and next the technique of treatment and the results.

If we classify cases entirely upon the clinical examination we will always find that statistics based upon such a grouping will be of little value, because we cannot compare the results obtained in the various groups in the various clinics. If we would adopt one classification, especially that of the Cancer Commission of the American College of Surgeons, then it would be possible to compare the results of all the clinics. If we read the results in the different clinics we will find a great difference of opinion. For example, what we call invasion of the parametrium, in Europe they call the

borderline case. Think of the difference in the results in the two sets of statistics. I wish we could have an absolutely rigid classification so that we could compare our results and know when to use surgery and when to use radiation therapy, and then which would be the best, the small dose, the large dose, or the combined treatment with radium and the roentgen rays, with either the low voltage or the high.

In the application of the technique we invariably take into consideration the pathology. We feel that this is necessary from the diagnostic standpoint as well as the prognostic, and also the application of the technique.

We all agree so thoroughly regarding the malignancy of any cervical carcinoma that I think we should take this into consideration in the treatment of these cases. We must in all cases calculate the dose for each and every patient. The radium dose in our technique is absolutely constant; we never change it. That is, the application cervically of 3600 to 4000 mg-hr. of radium. I think it makes little difference how much radium is used, so the dose is the same. If we use the applicators which I prepared, and place them in the pelvis, and estimate the radiation intensity at 100 per cent at 3 cm. distance from the radium capsule, this will drop to 10 per cent at the bony periphery. A permeation of the entire bony pelvis with radium is entirely impossible unless we can have the distribution of radium seeds or needles made by means of a laparotomy. In that way we might possibly obtain a radiation dose all through the pelvis.

The radium dose is constant but the roentgen-ray dose is changeable for different patients. When I look back over the cases of cervical carcinoma which I have treated by the combined method, I note that up to 1919 we used the small field method with filters of aluminum. After that we began to use large fields with copper filters and increased the skin distance. Since 1921 we have been using the high voltage therapy. I cannot say which of the three is the best method. I have obtained good results with all. I do not think my results at present are any better than they were, but there is this advantage, that if I use a high voltage tube, and particularly a water cooled tube, I shorten the duration of the treatment. The three fields do not take longer than fifty to seventy-five minutes. We do not do this on one day. We usually have the patient come in on Sunday or Monday. A careful examination is made to be absolutely sure of the findings. Then a piece of the tissue is removed for examination, and then the radium is inserted. There is never any difficulty in placing the radium. Depending upon the patient's condition this is left in for four days. If the patient is in bad general condition, or if within twenty-four to forty-eight hours she develops a severe reaction, vomits or something of that sort, the radium capsule is immediately withdrawn. In the average case we leave the radium in for four days, and on the last days of the week give the roentgen-ray treatment, so we usually complete the treatment in a week.

We pay particular attention to radiation sickness and the constitutional reaction. If we find that the constitutional reaction causes the patient to remain in the so-called negative phase of split protein reaction, then we try to stimulate that patient by using serum, milk protein or whatever we have, in order to have the patient get over the radiation sickness as soon as possible. If this does not suffice we resort to blood transfusion.

Dr. E. C. Samuel, New Orleans, La. I wish to say that since the presentation of my paper before this Society last year, we have treated 16 additional cases and out of the 16 there has been only one that could be considered of the so-called borderline type. The rest were absolutely inoperable. Unfortunately, we have those conditions in the South where ignorance exists, particularly in the rural districts, and consultation is the last thought of the patient. They come in only after the condition has existed for six to ten months before consulting a man who is competent to pass upon them. This probably influences our results.

Our technique has been the same as Dr. Schmitz has described. We have followed his example since we have been doing this work, but our opinion in regard to these inoperable cases has not changed from that of last year.

I do not agree with Dr. Brooks in regard to fistulae, for we have all seen the development of fistulae six, eight, or nine months after radium has been applied, without any local return of the growth.

Dr. James A. Corscaden, New York City. In our clinic we are still guilty of an occasional Wertheim operation. We do not approve of it but the pressure is so great that we would rather do it and control it than to have the patient go elsewhere. The cure of cancer should not be our only aim. In developing a technique, operative, radiation, or what-not, I think the palliations should be just as much considered as the cures. We should not say "cured," but "clinically well" for a certain period. If you like the five-year period, all right, but from then on we will all show a declining number.

Dr. William S. Stone, New York City. Dr. Schmitz has criticized our classification, which is proper, but the one point which

stands out is the fact that at the end of ten years we have obtained results from which it is recognized that there is no doubt that the best treatment for primary cancer of the cervix is radium and not operation. The statistics of the American College of Surgeons show that radium has produced as good results, at least, as surgery. I still think the clinical classification is the proper one. We lay much importance on the pathology. We know that we have to deal with the highly differentiated cell, the embryonic cells and those that are not so much differentiated, and we also know that the results in each class will differ.

Dr. George E. Pfahler, Philadelphia. One point I wish to discuss is a little different from the discussion which has preceded. I would urge every member to take an active part in the cancer control problem in educating the public to apply for treatment in the early stages of cancer. All the statistics show the great need of this, and we can serve as a unit of education just as well as anyone. It is our duty to do so.

I think we should treat any cases that we feel can be helped, even though we cannot get them well. The whole practice of medicine is based upon the fact that we help to prolong life, and we certainly have a right to prolong life by the treatment of carcinoma of the uterus with radium.

Dr. Leda J. Stacy, Rochester, Minn. I was interested in Dr. Healy's final conclusion regarding hysterectomy. At the Mayo Clinic our conclusions have been the same as his, that in the cases in which the operation could be done the patients did not need it, and that in the others it was impossible to do it.

Dr. Healy (closing). I greatly appreciate the discussion. We are all trying to get somewhere with the work in a very unhappy field. Unfortunately, I fear that most of these women will eventually die from cancer. Our statistics would tend to indicate that sooner or later cancer recurs somewhere. Nevertheless, we are doing a great deal to help our patients with a form of therapy that has practically no mortality associated with its proper use, and which restores them quickly as active members of the community for a considerable period of time.

There is no early symptomatology in cancer of the cervix or corpus uteri. There cannot be because bleeding is the only thing that calls attention to these lesions and that represents necrosis, which we cannot have in early lesions. I think we must educate the medical profession not to permit chronic inflammatory conditions of the cervix to remain untreated.

As to the microscopic pathology, in our 149 cases of cancer of the cervix last year, there were about 5 adenocarcinomata. All the others were epidermoid or squamous cell carcinoma, and we have been totally unable to figure out a plan of treatment based upon any variation in the cellular or basic structure of those squamous cell carcinomas. Whether they are small cell or polyhedral or what-not, our results remain practically the same in the entire group as regards those that improve under the treatment we carry out.

I disagree with Dr. Brooks in his statement regarding metastases. We seldom see metastases outside of the pelvis. We regard it as a local, recurrent disease. When we do a Wertheim operation we always find the metastases in the pelvis. We feel that we have a fine means of securing effects from radiation therapy because the disease remains for so long a time in the pelvis.

Our report includes all cases that have been treated, either in the palliative or the complete way. If a patient drops out of sight for any reason and we cannot locate that patient by the first of the following year, she is counted as dead in our list, so the statistics I gave you are probably correct.

As to the value of the roentgen ray in the parametrium, at the Memorial Hospital we have seen local lesions of the parametrium which appeared or which persisted after the first treatment disappear. There is no doubt that we can cause these parametrial growths to disappear.

SUGGESTIONS REGARDING RADIUM TREATMENT OF RECTOSIGMOID CARCINOMA*

BY JAMES T. CASE, M.D., F.A.C.S.

Battle Creek Sanitarium

BATTLE CREEK, MICHIGAN

ONLY those who have endeavored to make an accurate application of radium into rectosigmoid tumors above the reach of the proctoscope fully appreciate the great difficulties to be overcome. Radium-bearing rectal tubes or bougies nearly always double upon themselves, and even under the guidance of the roentgenoscope such a means of radium application is very unsatisfactory. It is difficult even in rectal cases where, with the patient in the knee-chest position, the introduction of the radium needles or tubes may be made under visual guidance. In inoperable cases, which have come to operation, the application of radium needles in some form or other may be feasible, but here again only the upper part of the growth is reached under visual guidance.

After all, the colostomy which sooner or later comes to be necessary in practically every case of rectosigmoid carcinoma is the best means of affording relief from pain. The diversion of the intestinal stream from the painful ulcerating area, whether or not stenosis is present, is, in the writer's opinion, a thing to be accomplished as early as possible in every case of rectosigmoid or rectal carcinoma just as soon as the inoperability of the case is determined.

It therefore seems logical as a routine to recommend operation in every case of this sort just as soon as the patient has been seen, having in mind a two-fold purpose: (1) to determine whether it is feasible to remove the tumor, and, if so, to remove it, and (2) if the tumor cannot be removed, to do a colostomy. The writer prefers one of the types of colostomy where the fecal stream is completely diverted, thus giving the tumor-bearing area absolute rest.

The writer's endeavors to make accurate application of radium in these colostomized cases has gradually led him to the adoption of the following technique:

(*a*) *Introduction of a Thread.* This is done as soon as feasible after the operation. Five or 6 feet of fine silk thread is wound off on to a spool and one end of the thread attached to the clothing; the other end of the thread is tied to a small bit of cotton or a piece of gauze sponge of such size as seems appropriate to the case. This sponge is dipped in pure glycerine (suggested by my colleague, Dr. W. F. Martin) and then by means of a small proctoscope or a long forceps, introduced as deeply as

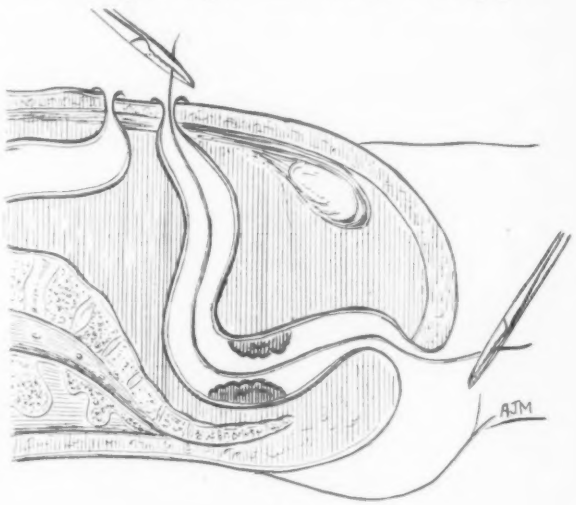

FIG. 1.

possible into the upper end of the excluded colon, that is, into the abdominal opening of the tumor-bearing loop. Under the powerful stimulus of pure glycerine on peristalsis, the bolus of gauze or cotton is usually carried promptly through the stricture into the rectum, and frequently it is expelled by the patient into a bedpan within one to two hours. The writer has thus far had only one patient with an extremely tight stricture where he was not able to pass the thread in this manner. Sometimes it requires twenty-four to forty-eight hours; usually two to three hours are sufficient.

* Read at the Tenth Annual Meeting, AMERICAN RADIUM SOCIETY, Atlantic City, N. J., May 25–26, 1925.

If the first attempt results in failure it is well to change the size of the gauze sponge. In a few cases I have succeeded in washing a small sponge through from the abdominal to the anal opening by means of irrigation. In this manner one is sometimes able to get a thread through where the passage of a tube or bougie is quite out of the question, aside from the danger of bowel perforation involved. The fine silk thread once through

FIG. 2.

should be used to draw from above downward a strong silk or linen thread which will not be in danger of breaking (Fig. 1).

(*b*) *Preparation of Radium Applicator.* From the previous roentgen examination, plus the data recorded at operation, excellent idea is formed of the exact shape and extent of the growth. A rubber tube 60 cm. in length with a lumen 4 or 5 mm. in

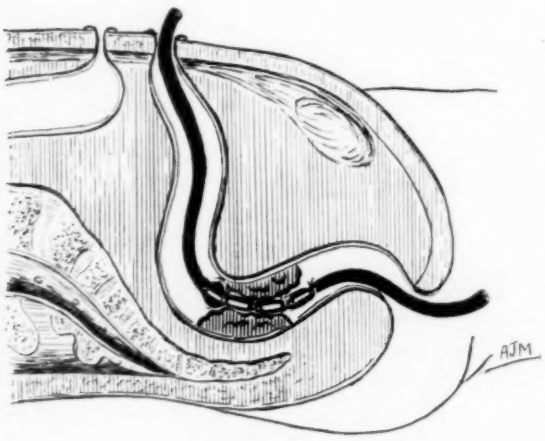

FIG. 3.

diameter is selected. Radium capsules in their usual silver and brass containers are then slipped inside this tube to a point which is approximately two-fifths of the distance from the lower end. These radium capsules are secured in place by tying threads around the tube in the manner suggested in Figure 2. Three or more capsules may thus be prepared for end-to-end application, depending upon the extent of the tumor.

The next point to be determined is how, when introducing the tube, to place the radium in contact with the tumor. Even under roentgenoscopic control this was difficult for the writer until he hit upon the following scheme:

Ordinary dental plastic rubber is cut into narrow strips, say 1 cm. wide, and a "hump" is produced at about the middle of the position of the uppermost capsule by winding this plastic rubber strip around the outside of the rubber tube. This makes a shoulder, whose total diameter is two and one-half or three times that of the rubber tube itself.

(*c*) *Introduction of Radium.* The application may be made with the patient in bed, or if further check is desired, upon the horizontal roentgenoscopic table. The patient had better lie upon the back with the knees separated. What is intended to be the lower end of the tube is tied to the upper end of the string and well lubricated with carbolated vaseline. By traction upon the caudal end of the string the rubber tube is thus pulled down into the abdominal opening of the tumor-bearing loop and carefully and slowly worked through until it emerges at the anus where it is seized with a pair of forceps. The operator, holding the two ends of the tube, one emerging from the abdominal and one from the anal end of the tumor-bearing loop, is then able to continue downward traction of the rubber tube until the shoulder or "hump" described in (*b*) impinges against the upper border of the stricture (Fig. 3). The operator thus has the assurance that the radium is in exact position; and by clamping the lower end of the tube close to the body, the tube may be left with the conviction that it will remain in proper place. At the conclusion of the treatment the lower forceps is removed and the tube is

extracted from the abdominal end of the excluded bowel.

The exact dosage in these cases depends upon the amount of filter in the preparation. In some cases with very tight stricture it is necessary to begin with a rubber tube of much smaller caliber than described—so small that it is impossible to put inside of it the radium with its usual covering of one millimeter of silver and one millimeter of brass. It may be necessary in these instances to modify the time of application very materially on account of the necessity of omitting part of the filter. This, however, may be done with perfect safety, the tube being left in a much shorter time at the first application. It is usually possible at subsequent applications to introduce a much larger tube containing radium capsules under the usual filter conditions.

The writer's present plan is to employ a lower radium value in the applicator and a correspondingly longer application, feeling that this gives best results. Statistical data upon this point are lacking because it is only in institutions where very large numbers of these cases are treated that proper comparisons can be made.

For applications into rectal carcinomas easily within reach of the proctoscope or anoscope it is not necessary to make such elaborate preparations. Nevertheless, one of the principles above described is useful in this situation when one wishes to place radium capsules in the lumen of the stricture. In these cases, when it is possible to intubate the stricture through a rectal speculum or a proctoscope, the writer first prepares a tube in the following manner:

A rather stiff tube of much smaller caliber is selected, one much too small to contain the radium capsule but quite large enough to allow the escape of gas or fluid from the bowel above the stricture. The radium capsules, one or more, are then bound on to the outside of this rubber tube with the thin strips of dental plastic rubber in such a manner as to make the total diameter of the applicator as small as possible. The whole applicator is then smoothed off with this plastic rubber in the best manner possible. When a colostomy has been done the necessity of using a canalized applicator of the type just mentioned no longer exists and here we may employ a tube of sufficient caliber to push the radium capsules into its lumen and fasten them there as described for rectosigmoid tumors.

The applicator having been prepared in either of the ways which seems more desirable, it is introduced into the rectum and into the lumen of the stricture at the point which by palpation and vision is deemed to be most accurate. A forceps is then applied on the tube just outside the external sphincter and the tube withdrawn, cleansed and dried. With other narrow strips of dental plastic rubber, already found so useful, two "humps" or shoulders are built up on the tube about 15 mm. apart at such a point that when the anal sphincters seize the tube between the two humps, the radium capsules will lie within the tumor. The patient is again placed in position on the table and the tube introduced under visual guidance, the sphincter being allowed to close on the tube between these two humps, thus assuring proper maintenance of the tube in position.

ABSTRACT OF DISCUSSION

Dr. George E. Binkley, New York City. All cases of carcinoma of the rectosigmoidal junction are obstructing. It is only a question of degree, and it is impossible to get along without a colostomy except in a few cases that will not stand the operation. Most persons object to it when it is first mentioned but it is usually not so bad as they fear it may be, and most patients after leaving the hospital do not complain much about the colostomy. Many of them do not wish to have it closed at the proper time. It is well worth the small amount of inconvenience it causes the patient. All cases should be gone over as carefully as possible before starting treatment, and the treatment should then be outlined and followed through. If a case is so far advanced that there is nothing to be gained but mild palliation, the colostomy may be done under local anesthesia.

It is true that many of the patients are relieved by surgery alone and many by radium alone, but perhaps the combined treatment is better than either one used singly. If it is thought beneficial, the irradiation may be started before the colostomy is done, and fol-

lowing the colostomy bare seeds can be implanted. When the abdomen is opened one should be prepared to do whatever may be found necessary.

It is rather difficult to irradiate the tumor and not irradiate many other tissues in the neighborhood. Most growths are not absolutely uniform above and below, and this may cause much difficulty. We have been using the string of tubes and the bare tubes. In some cases the first method is preferable, while in others the second is better. Dr. Case's method of application is most interesting. I have been placing the radium in position by means of the proctoscope, but in some cases with polyps it is impossible to get the radium just where you want it. By tactile sense in some cases you can outline the tumor and distribute the radium equally. In those cases we use external radiation by roentgen rays or radium pack.

We should guard against overtreatment. Many patients with carcinoma in the lower bowel are put through very severe treatment when the condition is beyond hope. We may develop a technique by which we can accomplish more, but at present I do not see the necessity for taking on very advanced cases and irradiating them and making the patients worse. I think all cases should be classified and treated accordingly.

STATISTICAL STUDY OF RADIATION THERAPY IN EIGHT HUNDRED AND ONE CASES OF CARCINOMA OF THE BREAST*

BY G. E. PFAHLER, M.D., AND B. P. WIDMANN, M.D.

PHILADELPHIA, PENNSYLVANIA

THE object of this study is to determine the relative value of radiation therapy in carcinoma of the breast, extending over a period of twenty-five years. The technique during this period of time has, of course, varied from that of no filtration and low voltages to that of 0.5 mm. of copper filtration and 200,000 volts. Because of the length of this paper, we have been compelled to omit the detailed discussion of technique. The varying technique has been described in previous papers, and will be reviewed at some future date.

A statistical study of the therapeutic results in carcinoma is always difficult because of the variable factors involved and the great difficulty of classification. Unfortunately, the great majority of the patients with carcinoma of the breast who are referred to the radiologist are in the inoperable, and very far advanced stages. Dr. Mayo says, "In this type of case, radiotherapy is at its best a triumph and a despair. It often does so much good that the patient and the family begin to look for a cure, but failure is the result, and radiotherapy is unjustly brought into disrepute for a meritorious performance."

A direct comparison with surgical statistics is difficult because very few primary cases have been referred for treatment. In the great majority of instances, only the inoperable cases have been referred for primary treatment, and only the advanced cases for postoperative treatment. Recurrent carcinoma, which makes up a great part of our cases, is not even included in the usual surgical statistics.

The great variation in the extent of the disease, either primary or recurrent, together with the variability in the degree of malignancy, and the sensitivity to radiation makes classification extremely difficult. We have, therefore, made use of numerous tables to determine the values under various circumstances. It is well known that in all surgical clinics many patients are not treated at all, and, therefore, are not included in the surgical statistics, while practically all cases are treated by radiation and we have therefore included them.

In most surgical statistics, the cases are classified on the basis of operability. Practically all surgical clinics, today, consider tumor tissue which is movable

* Read at the Twenty-sixth Annual Meeting, AMERICAN ROENTGEN RAY SOCIETY, Washington, D. C., Sept. 22–25, 1925.

and confined to the breast as operable. Many clinics still consider carcinoma which has extended to the axilla as operable. Practically none consider a case with supraclavicular involvement as operable. The end results are affected not only by the type of cancer, but by the age of the patient, the stage and rapidity of growth, extent of metastasis, regions invaded, the physical resistance of the patient, duration of the symptoms before operation, and by the period of time that elapses between operation and radiation, also by the duration of the recurrence.

In order to get some data about these types of cases that we are called upon to treat, we classified 701 from Dr. Pfahler's private clinic (1900–1925) including a series of 100 unselected, consecutive cases from the records of the Medico-Chirurgical Hospital, totalling 801 cases.

The classification of cases according to age, duration of disease, extent of involvement, etc., is as follows:

TABLE I

11 Males	Married 595 or 74%
790 Females	Single 194 or 26%
801 Total	
Right breast involved in 403 cases or 51%	
Left breast involved in 361 cases or 45%	
Both breasts involved in 37 cases or 4%	
801	

Fifty-three per cent of the cases gave a history of a lump as the first sign to attract their attention. A history of injury was given by only 14 per cent, pain by 21 per cent; the remaining 12 per cent presented such symptoms as bleeding from the nipple, eczema, anemia, etc., as enumerated in Table II.

TABLE II

INITIAL SYMPTOMS

Lump 53% of cases	Increase size breast
Pain 21% of cases	Lump in axilla
Injury 14% of cases	Lump in neck
The remaining 12% complained of one or more of the following initial symptoms.	Abscessed breast
	Tender axilla-neck
	Dimpled skin
	Sinus in breast
Stinging sensations	Pigmented mole
Eczema nipple	Pain right under abdomen
Bleeding nipple	Rheumatism back, etc.
Discharge nipple	Swollen arm
Ulceration nipple	Cough
Soreness nipple	Dyspnea
Retraction nipple	Cachexia
	Anemia

More cases occurred between forty and fifty years of age than at any other period of equal length. The youngest patient was sixteen years of age; the oldest, eighty-seven years of age.

TABLE III

AGE INCIDENCE

Years	No. Cases	Years	No. Cases
16	1	55–60	113
18	1	60–65	81
20–30	20	65–70	41
30–40	79	70–75	32
40–45	124	75–80	16
45–50	161	80–90	2
50–55	130		Total 801

Pathological reports were obtained in 605 cases. In 109 cases no biopsy was made because the condition was clearly malignant and inoperable. Of the remaining 93 cases, 37 were recurrent and metastatic so that 56 or 6.9 per cent of the total might have the diagnosis disputed, excepting on clinical evidence; in these, operation was contraindicated or definitely refused; 505 or 62 per cent were recurrent, metastatic, and inoperable cases, and therefore would have needed no microscopical confirmation. "Fibroadenoma" was diagnosed microscopically in 22 cases. Of these, 18 had been sent to us some time after the operation on account of recurrences or metastatic carcinoma. In some of these, restudy of the slides showed carcinoma in the original sections. In others, sections of the recurrent lesions showed carcinoma. The 4 remaining cases are not included in the subsequent tables.

"Benign tumor" and "cystic mastitis" was reported in 11 cases. All of these cases were sent to us for treatment later because of recurrence or metastases. It is self-evident that none of these cases are sent to us for postoperative irradiation treatment until after the microscopical study; and that a "benign" case, without clinical evidence of disease, would not be sent. These facts are given not for criticism, but to show that not only a clinical diagnosis of "benign" disease may be in error, but even a microscopical study may miss the malignant portion.

The case of "chronic sinus following abscess" was sent to us for roentgen-ray treatment on account of metastatic disease.

TABLE IV

HISTOLOGICAL CLASSIFICATION

	No. Cases
None obtained (including prim. op.)	93
None made (inop. prim. & recur.)	109
"Carcinoma"	216
"Malignant"	114
* "Fibroadenoma" (18 of these sent to us because of later recurrence and metastasis)	22
Colloid carcinoma	2
Paget's disease	7
Adenocarcinoma	57
Medullary carcinoma	12
Scirrhous carcinoma	113
Carcinoma simplex	19
"Benign tumor" (sent to us later on account of recurrence and metastasis	11
Spindle cell sarcoma	1
Melanotic sarcoma	4
Sarcoma	5
Chronic sinus following abscess	1
Basal cell carcinoma	1
Carcinoma en currasse	17
Papilliferous cyst carcinoma	1
Total	805

* 4 cases of true fibroadenoma not classified in statistics.

The average time between the patient's discovery of the breast condition and operation was seventeen months. This estimation included the early and advanced cases. The shortest time was one week and the longest time was ten years. Only 33 cases, or 4 per cent, applied for any kind of treatment within four weeks after recognizing trouble. The average time for the inoperable cases from the first recognition of symptoms to treatment was approximately twenty-one months. During recent years, education of the public has greatly diminished the length of time from the recognition of symptoms to treatment. Ewing places the average at about 13.28 months. Greenough, in the latest report of the Massachusetts General Hospital, showed an average of 7.5 months in cases studied from 1918–1920, inclusive, illustrating the value of educating the public to report for early treatment. The average duration of symptoms preceding operation and roentgen treatment (seventeen months) as indicated above, in itself shows that in our clinic we have been dealing with very advanced cases.

The average duration of time from operation to beginning of roentgen treatment was 10.5 months. This estimation was made from the private office patients only, because a more accurate average could be obtained from the more complete records; 559 of these patients show sufficiently accurate records to give the above average. This long period also indicates the advanced type of cases with which we have had to work.

TABLE V

DURATION OF SYMPTOMS BEFORE PATIENT APPLIED FOR ANY KIND OF TREATMENT

(Average 17 months)

	No. Cases
Less than one month	33
1 to 6 months	207
6 mos.–1 year	241
1–2 years	132
2–3 years	106
3–5 years	34
5 years	17
6 years	11
7 years	6
8 years	7
9 years	4
Over 10 years	3
Total	801

TABLE VI

AVERAGE TIME INTERVENING BETWEEN OPERATION AND ROENTGEN TREATMENT (10.5 MOS.)

Treatment Started	No. Cases	Treatment Started	No. Cases
2 weeks	67	12 months	39
3 weeks	11	1½ years	44
4 weeks	31	2 years	20
5 weeks	17	3 years	24
6 weeks	23	4 years	23
		5 years	4
7 weeks	18	6 years	4
8 weeks	30		
3 months	25	7 years	3
4 months	23	8 years	2
5 months	19	9 years	1
6 months	34	10 years	1
7 months	10	11 years	1
8 months	18	14 years	1
9 months	15		
10 months	33	Total	559
11 months	18		

Unless a patient is referred for roentgen-ray treatment within four weeks after operation, it cannot be regarded as true "postoperative" treatment. Only 109, or 19 per cent, of the above 559 cases belong, therefore, to the postoperative group.

The average period of time from operation to the time at which the patients noticed recurrence and were referred for treatment was one year and four months. This is based upon a study of 225 cases in which the records were sufficiently complete; *125, or 56 per cent, of these cases recurred within six months.* This further illustrates the advanced or virulent type

of case which is operated upon and then referred later for roentgen treatment. Bunts, in reporting 600 cases, finds 28.5 per cent recurred within six months. When patients show supraclavicular involvement within two to eight weeks after operation, we believe that these metastases were present, even if not palpable, before operation.

TABLE VII

AVERAGE TIME DURATION FROM OPERATION TO RECURRENCE (1 YEAR–4 MONTHS)

Recurrence within	Cases	Recurrence within	Cases
1 week	4	12 months	19
2 weeks	13	1½ years	4
3 weeks	6	2 years	16
4 weeks	21	3 years	13
5 weeks	4	4 years	3
6 weeks	22	5 years	5
7 weeks	3	6 years	6
8 weeks	8	7 years	2
3 months	11	8 years	4
4 months	10	9 years	2
5 months	7	10 years	1
6 months	16	11 years	1
7 months	6	13 years	1
8 months	4	18 years	1
9 months	4		
10 months	5	Total	225
11 months	3		

The classification of the types of cases and extent of involvement in 801 cases are shown in Table VIII; 505, or 63 per cent, of these cases (*c* and *d*) were primary inoperable, recurrent and metastatic; 342 cases, or 43 per cent, of the 801 were advanced recurrent cases with metastasis to glands and chest; 163, or 20 per cent, were primary inoperable cases. This 20 per cent group includes all cases with fixation of the tumor to the skin or chest wall, with involvement of the axillary and supraclavicular glands and frequently the mediastinum. Of these 342 recurrent cases, 219, or 67 per cent, showed demonstrable roentgen evidence of disease in the mediastinum at the beginning of roentgen treatment. Of the 163 primary inoperable cases 114, or 69 per cent, showed mediastinal involvement at the beginning of the treatment; 45, or 5.5 per cent, of the advanced cases showed bone metastasis at the beginning of treatment. This percentage of bone involvement is considerably higher today because the investigations are more thorough and complete than they were in the earlier days.

TABLE VIII

CLASSIFICATION OF TYPES AND EXTENT OF INVOLVEMENT IN 801 CASES (701 OFFICE PATIENTS PLUS 100 PATIENTS FROM THE M.C. HOSPITAL)

	Cases	Per Cent
a. Preoperative and postoperative cases	49	6
b. Postoperative	193	24
c. Recurrent metas. glands and chest	342	43
d. Primary inoperable cases	163	20
e. Primary operable, refused or contraindicated	54	7
Total	801	100

TABLE IX

CLASSIFICATION OF TYPES AND EXTENT OF INVOLVEMENT IN 701 PRIVATE OFFICE CASES

	Group	Before Operation Glands	After Operation Glands	No. Cases	Per Cent
a. Both Preoperative and Postoperative Treatment					
A	I	No	No	8	18
B	II	Yes	No	24	56
C	IV	No	Yes (not removable)	2	5
D	IV	Yes	Yes (not removable)	9	21
			Total	43	6
b. Postoperative Treatment					
E	II	Yes	No	86	49
F	IV	Yes	Yes	63	36
G	I	No	No	22	13
H	IV	No	Yes	3	2
			Total	174	25
c. Recurrent Cases					
I	III	Local Recurrence		13	4
J	IV	Local rec. glands, ax. and supcla. regions		43	15
K	IV	No loc. rec., metas. mediastinum-lungs		13	4
L	IV	Loc. rec. ax. supcla. and mediastinal		199	67
M	IV	No. loc. metas. to spine and other bones		7	2
N	IV	Metastasis-mediastinum, lungs and bones		23	8
		Total		298	43
d. Primary Inoperable Cases					
O	IV	Fix. sk. or ch., ax., s. cl. and medias. dis.		117	82
P	IV	Fix. sk. or ch., ax., s. cl. plus bone metas.		5	3
Q	IV	Made operable without chest metas.		13	10
R	IV	Made operable with chest (palliative)		5	3
S	IV	Removed by electrocoagulation		3	2
		Total		143	20
e. Primary Operable Cases					
V	I	Prim. operable (refused phys. not fit)		43	6
T	I	Prim. operable questionably maglignant 12 or 2%			
		Total		701	

The groups under each subdivision are classified after the fashion of the generally accepted surgical tables.

Group I ..... *Early* operable—no glands involved.
Group II ..... *Late* operable with glands involved.
Group III ..... Local recurrence—operable.
Group IV ..... Inoperable—primary and secondary.

It will be seen in Table VIII that only 37 per cent of the total of 801 cases were in any sense surgical, and form the only group that can be compared with surgical statistics, leaving 63 per cent that must be either abandoned or treated by radiation.

It will be seen that the relative percentages remain the same whether the hospital group is added or not.

In the "preoperative and the postoperative group" (a), glands were involved in 35 cases, or 82 per cent, leaving only 8 cases, or 18 per cent, with no gland involvement.

In the "postoperative group" (b), glands were involved in 152 cases, preceding operation, or 87 per cent, leaving 22, or 13 per cent, with no gland involvement. Considering the three groups (A-G-V) it will be seen that only 73 cases, or 10 per cent, of the total of 701 cases in our previous records came under treatment before glands were palpable.

In the recurrent group (c), 199, or 67 per cent, showed axillary, supraclavicular and mediastinal disease.

In the primary inoperable group (d), of 143 cases, 107, or 71 per cent, showed demonstrable roentgen evidence of metastasis in the chest at the beginning of the roentgen treatment; while 5 cases, or 3 per cent, revealed bone metastasis.

In the primary operable group (e), 43, or 6 per cent, received radiation treatment without operation. These cases refused operation or were physically unfit; 12, or 2 per cent, were questionably malignant. In all instances surgery was advised; 2 of the questionable cases went to operation three and five months after our first examination, and both died of fulminating metastatic carcinoma within six months. These cases seemed to develop rapidly before treatment, and were only held at a stand-still for a time by treatment.

ESTIMATION OF LIFE IN MAMMARY CANCER WITH RADIATION THERAPY

We have classified these cases in the preceding tables in such manner that they can be compared with surgical treatment, and with *no* treatment, with regard to the total duration of life from the beginning of disease.

TABLE X

CASES TREATED IN THE OFFICE UP TO THE PRESENT TIME GROUPED ACCORDING TO YEARS TREATED

Year	Cases	Year	Cases	
1900	2	1916	22	
1901	1	1917	31	
1902	3	1918	48	
1903	9	1919	48	
1904	13	1920	57	
1905	15			
1906	12			496
1907	21	1921	46	
1908	22	1922	48	590
1909	33			
1910	19	1923	56	
1911	31	1924	28	
1912	29	1925	27	(5 mos.)
1913	20			
1914	24	Total	701	
1915	36			

496 cases were analysed from 1900–1920, inclusive.
590 cases were analysed from 1900–1922, inclusive.

When a patient was no longer traceable we recorded the case as having lived so many years to the time of the last record. Every case is entered, and every case applying for treatment is included in the statistics, whether the patient was treated, refused to complete treatment, was hopeless from any standpoint of treatment, or the records were incomplete because we could not follow the case to its termination. We therefore recorded a case as automatically dead when no longer traceable. This, however, has not always been the case and may not give radiation its full value, because frequently some of these cases will return for inspection several years later, free from all palpable evidence of the disease. We believe this will balance any discrepancies that might be weighed against the element of the personal equation in interpreting end results in this study. Twenty cases were so far advanced that no treatment or only a partial series of a treatment was given. The average length of life in these cases was three to five months from the time of our examination, consequently reducing the total values.

Table XI itemizes the duration of life of each group according to the classification shown in Table IX. The duration of life of all cases in all groups is summarized in Table XII for the three and five year periods.

Of all cases, early and late, operable and advanced, inoperable and recurrent, 50 per

TABLE XI
DURATION OF LIFE AFTER BEGINNING TREATMENT (TABLE IX)
(590 cases, 1900–1922)

A	Group	Mo. 6	Mo. 8	Number Years Alive 1	1½	2	2½	3	3½	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	Total
a. Both Preoperative and Postoperative Treatment																											
A	I	–	..	..	..	–	1	1	..	3	2	..	..	–	..	..	..	..	..	..	..	..	..	..	..	1	8
B	II	..	..	..	..	..	3	2	1	..	2	1	1	1	..	..	..	..	2	..	..	..	..	..	..	..	13
C	IV	..	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1
D	IV	1	..	..	3	..	2	1	..	1	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	9
b. Postoperative Treatment																											
E	II	..	3	6	4	7	3	6	6	2	10	5	1	2	1	3	1	2	1	1	1	1	..	..	1	1	68
F	IV	2	6	5	12	3	1	5	1	2	4	4	–	..	..	1	1	..	..	2	..	..	..	2	..	..	51
G	I	1	..	1	1	1	..	1	..	–	3	2	4	..	..	1	..	..	2	2	1	2	..	..	..	..	22
H	IV	..	..	1	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	..	..	..	3
c. Recurrent Cases																											
I	II	..	1	1	..	2	..	..	..	2	..	1	..	..	2	..	..	1	1	..	1	1	..	..	..	..	13
J	IV	1	1	4	4	3	..	6	1	4	..	1	..	2	..	1	..	..	..	1	1	..	1	..	..	1	32
K	IV	1	1	1	..	3	..	1	1	..	2	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	10
L	IV	20	27	31	8	21	1	18	17	14	11	2	1	..	1	1	1	..	..	..	..	..	..	1	..	..	175
M	IV	1	1	..	..	1	..	1	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	5
N	IV	..	8	6	..	1	..	1	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	17
d. Primary Inoperable Cases																											
O	IV	10	12	13	8	11	5	10	7	6	3	4	2	2	1	2	3	..	..	3	..	..	..	..	..	..	102
P	IV	..	2	..	1	1	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	5
Q	IV	1	1	3	..	..	..	..	2	..	1	..	..	..	1	..	1	..	2	..	..	..	..	1	..	..	13
R	IV	..	1	2	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	4
S	IV	..	..	1	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	2
e. Primary Operable Cases																											
V	I	..	..	1	1	1	2	4	1	1	4	2	2	1	1	2	1	1	3	1	..	..	..	..	..	..	29
T	I	..	..	..	..	..	..	1	1	..	1	1	..	..	..	1	1	..	1	..	1	..	..	..	..	..	8
		38	64	76	42	55	21	60	38	37	44	23	11	8	7	12	9	4	12	10	5	4	2	4	1	3	590

cent were alive three years, and 27 per cent alive five years or more.

In the postoperative group (G), *without gland involvement, 81 per cent were alive three years, and 77 per cent alive five years or more.*

In the postoperative group (E.F.H.), *with gland involvement, 56 per cent were alive three years, and 38 per cent were five years or more.*

Of the cases receiving both preoperative and postoperative treatment (a), without gland involvement, 87 per cent were alive three years and 37 per cent alive five years or more. These cases had advanced ulcerating local disease.

In preoperative and postoperative group (B-C-D) with gland involvement, 30 per cent were alive three years and 18 per cent alive five years or more. The records of (B-C-D) show advanced cases, and operations and roentgen treatment in many instances were only intended as palliative. Many of these cases today would be classed as totally "inoperable." This explains why the percentages are lower than when only postoperative treatment was used.

The local recurrent operable group (1) shows 69 per cent alive three years, and 54 per cent alive five years or more. This observation is important to contrast with the usual experience of fulminating recurrences and metastasis which are so frequent after excision. In our group of recurrent cases (c) there were:

34 cases with histories of one operation before coming to us
19 cases with histories of two operations before coming to us
8 cases with histories of three operations before coming to us
5 cases with histories of four operations before coming to us
4 cases with histories of five operations before coming to us

70

TABLE XII

TOTALS OF TABLE XI—THREE AND FIVE YEAR AVERAGES

a. Both Preoperative and Postoperative Treatment

		Total	Alive 3 Years	Per Cent	Alive 5 Yr. or More	Per Cent
A	I	8	7	87	3	37
B	II	13	10	77	7	54
C	IV	1	0	0	0	0
D	IV	9	3	33	1	11
		b. Postoperative Treatment				
E	IV	68	45	66	31	45
F	IV	51	22	43	14	27
G	I	22	18	81	17	77
H	IV	3	2	66	1	33
		c. Recurrent Cases				
I	III	13	9	69	7	54
J	IV	32	19	59	8	25
K	IV	10	4	40	2	20
L	IV	175	67	38	18	10
M	IV	5	2	40	0	0
N	IV	17	1	6	0	0
		d. Primary Inoperable Cases				
O	IV	102	43	42	20	19
P	IV	5	0	0	0	0
Q	IV	13	8	69	6	46
R	IV	4	1	25	0	0
S	IV	2	0	0	0	0
		e. Primary Operable Cases				
V	I	29	24	82	19	65
T	I	8	8	100	6	75
V. & T		590 37	293 32	50 86	160 25	27 68

For comparison with the usual surgical longevity tables the following grouping quickly summarizes the radiation values.

Group		Total Cases	Alive 3 Yrs.	Per Cent	Alive 5 Yrs.	Per Cent
I	Early operable—no glands	67	57	85	45	68
II	Late operable with glands	81	55	68	38	46
III	Recurrent operable	13	9	69	7	54
IV	Advanced rec. and metas. and prim. inop	429	172	40	70	16
	Total	590	293	50	160	27

Ewing states that statistics favor the conclusion that operation, on the whole, shortens life in the recurrent cases and in the great majority aggravates the suffering.

In the advanced recurrent and metastatic group (J-K-L-M-N) out of 239 cases, 93, or 38 per cent, were alive three years, and 28, or 12 per cent, alive five years or more. These cases as a whole are so advanced that practically they may be considered as being in the terminal stages of the disease at beginning treatment. The above group of 70 cases with rapid recurrences following operation is an example of the late stage of the disease in which they come for radiation treatment. Of these 239 cases, 216, or 72 per cent, of this group showed demonstrable roentgen-ray evidence of mediastinal metastasis at the beginning of roentgen treatment. The average life of this group after commencing roentgen treatment was two years and nine months (Table XI.) If we add to this the average time from operation to recurrence, which was one year and four months, we have a duration of life of four years and one month from the time of the operation. The average time from the discovery of the lump to operation was one year and five months, making a total duration of life from the first recognition of the disease to its termination of five years and six months in these advanced, recurrent and metastatic cases. This estimation includes 20 cases in which the disease was so far advanced that no treatment was given or only slight treatment as a placebo, also 67 cases in which radiation could not be properly given. If these were eliminated, the average life after treatment would be approximately three years.

The advanced primary inoperable group (O-P-Q-R-S) show, in 126 cases, 41 per cent alive three or more years, and 20 per cent alive five years or more; 93 cases, or 73 per cent, of this group showed demonstrable roentgen-ray evidence of metastasis in the chest or bones, at the beginning of treatment. Yet the average duration of life from the beginning of roentgen treatment was three years and four months (Table XI). The time from the first recognition of the disease to roentgen treatment, in this advanced group, averaged twenty-one months, in 143 of 801 cases so analyzed. Therefore, with radiation treatment we have a duration of life from the beginning of the disease to its termination, in this advanced inoperable group, of five years and one month, or sixty-one months. Lee and Herendeen, in 57 cases which they class as "less advanced primary inoperable" carcinoma of the breast, find an average duration of life from the time the growth was discovered to be four years, or forty-eight months, with proper radiation.

Finney, in Keen's surgery, gives the average duration of life in the untreated

cases as twenty to twenty-eight months from the beginning of the disease. Sprengle, Odekop, Sibley, and Paget, quoted by Ewing, have estimated twenty-seven, twenty-nine, thirty-four and forty-eight months, respectively, as the duration of life in the unoperated cases.

Thirteen cases, (1.3 per cent), of our inoperable primary group, with no demonstrable mediastinal disease, became operable under radiation and give an average life of six years.

In the early primary operable group (V-T), 37 cases, or 86 per cent, were alive three years, and 68 per cent were alive five years or more from radiation treatment alone. This group flatly refused operation, or there were surgical contraindications to operation. Eight cases, or 1.3 per cent of this group (590 cases) might be regarded as questionably malignant, but the clinical course in all instances would have warranted operation.

An analysis of Tables XI and XII indicates very clearly the great advantage of radiation therapy in carcinoma of the breast; not only as an adjunct to surgery, but in the hopeless recurrent and inoperable cases. A relative comparison with the surgical groupings is possible only in the operable cases.

TABLE XIII

COMPARATIVE VALUES OF OTHER CLINICS AND METHODS (OPERABLE CASES)

		Alive 3 Years		Alive 5 Years	
		No Glands, Per Cent	With Glands, Per Cent	No Glands, Per Cent	With Glands, Per Cent
Greenough	Surgery	47	19		
König	Surgery	..	..	100	39
Bloodgood	Surgery	..	..	70	20
Lee	Surgery	..	..	...	15
Finsterer	Surgery	..	..	...	4.3
Doederlein	Surgery	..	..	46	5
Doederlein	Surgery and radiation not completed			48	20
Doederlein	Surgery and radiation totally completed			80 48	36
Wintz	Surgery and radiation both groups 77%				
Schmitz	Surgery and radiation			64	42
Pfahler & Widmann	Surgery and radiation			68	46

Table XIII shows that surgery of various clinics report from 46 to 100 per cent in the early operable cases and from 4 to 39 per cent in the cases where the glands are involved. Ewing believes that 4.5 per cent for five year cures represents the average success obtained by surgical treatment. Seuffert, Schmitz, Pfahler and Widmann show 36, 42 and 46 per cent, respectively, in the radiation treatment of cases showing gland involvement.

The recurrent cases with glandular and mediastinal metastasis show a postoperative life of forty-nine months with radiation. Handley and Greenough report an average life of 29.6, and twenty-five months, respectively, in the late cases with surgery alone. From first recognition of disease, the average duration of life with radiation in this recurrent group is five years and six months.

The inoperable primary cases show an average life of five years and one month, against twenty-seven, twenty-nine, thirty-four and forty-eight months in untreated cases reported by Sprengle, Odekop, Sibley and Paget.

In addition to increasing the duration of life, we, as well as others, have repeatedly demonstrated definite value of radiation in the advanced cases. The palliation, retardation and relief of suffering can only be appreciated by those who live in this work.

Murphy, Nakahara, Nogier, Jaubert, Colwell, Chambers, Wedd, and Russ, and many others, have adduced sufficient experimental data to establish radiation treatment as of value in conjunction with breast surgery. Everyone recognizes the value of radiation treatment in the advanced case. Why should it not be of value in the early case?

The great variation in response of many of these cases to treatment may be explained by the investigations of Broders and MacCarty on cell differentiation (lymphocytic infiltration, fibrosis, hyalinization and cellular differentiation). It is suggested that these factors play a significant rôle in the defensive mechanism against cancer, and recently they applied this method in a study of the longevity of cancer patients. It is possible that radiation may produce just such alterations in the tissues, as has been demonstrated recently by Earnst and his co-workers.

The end results in carcinoma of the breast, as in any other location of the body,

depend upon its early recognition and early treatment. It is only reasonable that the patient is likely to have a longer duration of life if radiation treatment can be instituted early, at most two to four weeks after operation. Recurrences are probably manifestations of a general dissemination. When glands are palpable, we must consider that there are probably many microscopic nests farther on in the lymphatic chain. At this stage no form of treatment will always cure, any more than tetanus or diphtheria antitoxin will cure tetanus or diphtheria in its terminal stages.

In conclusion, we believe that the radiologist has the same factors to consider as the surgeon, as expressed by Ewing, who says, "In mammary cancer, surgery meets with more peculiar difficulties and uncertainties than with almost any other form of the disease. The anatomical types of the disease are so numerous, the variations in the clinical course so wide, the paths of dissemination so free and diverse, the difficulties of determining the actual conditions so complex, and the sacrifice of tissue so great, as to render impossible in a majority of cases a reasonably accurate adjustment of means to ends." These same factors complicate the classification of mammary cancer for the radiologist, so that comparative statistics must take into account not only the duration of the disease before and after operation, but also the extent of involvement, and even then conclusions at best can be only relative. Radiation has not only proven its value, but its necessity in mammary cancer. The cooperation of the surgeon, internist and radiologist is vital. Experience and enthusiasm are prerequisites, and its practice just as much an art as any other specialty in medicine.

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DISCUSSION

Dr. Burton J. Lee, New York City. I think it is obvious to all of us that this has been a very extensive study and one which will be quoted extensively. Here is a very large group of cases which have been followed from every angle statistically, and I certainly congratulate Dr. Pfahler and his coworker on the extensive and far-reaching way in which the subject has been handled.

I will confine my remarks this morning to just a few phases of the subject, as it is quite impossible to discuss adequately very many parts of his paper which do need discussion.

Dr. Pfahler said something about educating the public, and it occurs to me that we ought to emphasize here the relation of the general practitioner to the subject of cancer of the breast. The first approach of every patient suffering with a tumor of the breast to medicine

is the general practitioner, and it is his decision which is usually final, and if his decision is an incorrect one, the patient is often doomed. I think our effort should be as much to educate the general medical profession as the public. It seems to me that the job rather lies in each general practitioner educating his own patients as to the necessity for frequent examinations and the significance of any breast symptoms of any sort. Where a society of this sort can enter into that chain is in its contact with general practitioners, endeavoring to point out to them the grave responsibility which is theirs and the peculiar strategic importance of their position; that it must be their decision which brings the patient for early care.

The statistics yielded several very interesting things. Among others, that there are as many cases in the decade from twenty to thirty as in the half decade from sixty to sixty-five. I don't think we usually appreciate that there is such a large number below thirty. It is really quite a frequent disease in that decade.

It is perfectly evident to all of us, with this paper before us, that the evidence for radiation as an efficient agent in the treatment of this disease seems rather beyond question. I feel, however, that we ought more and more to focus upon the life history of the disease uninterfered with by radiation or surgery, and I find it very difficult—and I imagine Dr. Pfahler has also—to get adequate data of any sort on this subject. Dr. Pfahler quoted—from Dr. Finney, I think—twenty-eight months as being the normal life period of carcinoma of the breast uninterfered with. There is no group of cases of sufficient number from which any conclusions may be drawn at present, it seems to me, and I believe our effort in a society of this sort and in similar societies, should be to gather all data we can concerning cases of carcinoma of the breast which have not been treated by any means. I have often mentioned one or two cases that have come to my notice at the Memorial Hospital, one a woman in whom the whole course of the disease was finished in five weeks, when she was dead, without treatment, and another that lasted 22½ years and wandered into the clinic one morning with advanced carcinoma of both breasts, which had never been treated; she had never seen the doctor, and she was really very well nourished at that time. She died six months later of internal metastasis.

I feel that we will have a more intelligent impression of what radiation can do, the more we know about the life history of the disease, and I ask the members of this Society to endeavor to gather data of this sort, which will be very useful in judging as to the efficacy of any form of treatment.

A word about the comparison of radiation with surgery in the treatment of this disease. Rather recently I was bold enough to report a small series of cases, at the Congress in London, of primary operable carcinoma of the breast treated entirely by radiation. All of these cases came to the clinic in 1920; there were only eight of them. The group was too small to be conclusive, but merely suggestive, perhaps. Of that group, there were six still alive, with no active evidence of disease, in 1925, which is almost five years from the beginning of treatment—which I think is suggestive and interesting. We are endeavoring to add to that group, so that we may have possibly some additional data which will allow us to compare pure radiation treatment with surgery.

Then, speaking for a moment of the preoperative and postoperative groups, and the operative alone. You probably are familiar with a communication that Dr. Herendeen and I made upon this subject, and there again we had only a small group of cases. We were able to obtain three comparable groups: one a pure surgical group, one a preoperative and surgical group and one a surgical and postoperative. The cases were all three-year cases, being the only ones we could properly compare. We had altogether 85 cases. Our figures, eliminating all cases with pathology which were not well advanced malignantly, showing 46 per cent alive were those treated with preoperative and postoperative radiation, and 30 per cent alive were those treated with postoperative radiation.

There again we had only a small group of cases.

One other word concerning the pathology—and I, with all modesty, call Dr. Pfahler's attention to this, because I feel that articles of this sort, put out by this Society, are sought for and studied with great scrutiny by surgeons throughout the country.

I find that surgeons are keenly interested in the present status of radiation in the treatment of carcinoma, and they are very exact in their scrutiny of our articles. I simply beg to call Dr. Pfahler's attention to the fact that in this group of 801 cases—I think it is quite inadvertent that he has not noticed it—there are quite a number of benign tumors included, and it does seem to me that they should be excluded from the study, because the paper is too valuable to have any possible source of error of that sort creep into it. For instance, there are 11 cases of benign lesions, one case of cystic mastitis, one case of a sinus following abscess of the breast, a case of tuberculous breast; and in addition to that there are a number of malignant lesions of

the breast—sarcoma, melanoma—which I think had best be kept in a group by themselves, to make the paper reach its full value.

DR. JAMES EWING, New York City. I don't know that I can say anything that is worth saying in the discussion, but I am willing to confess my very great interest in it.

Dr. Pfahler was kind enough to quote a statement I made regarding the application of surgical methods to mammary cancer. I have worked over the language in that statement very carefully now for several years, and I am not willing to change any of the wording.

I have always felt that the medical profession and the public demanded some other method of dealing with mammary cancer, and therefore I have been greatly interested in seeing the progress of radiation therapy in all forms of mammary cancer.

Nevertheless, at present my feeling is one of considerable disappointment on the whole regarding the results of recurrent and established cancer from radiation. There are many results that we see, and this report of Dr. Pfahler's is one that is increasingly encouraging, but the number of cases that go back and the great difficulty of deciding whether our treatment has actually followed the natural course of the disease, as Dr. Lee has pointed out, leads me to believe that there is much to be accomplished.

I believe the point that Dr. Lee made regarding the natural history of the disease is greatly underestimated, by all statistical studies, for the treatment of mammary cancer. It is very difficult to impress upon surgeons, less so perhaps upon radiologists, that the different kinds of mammary cancer in their natural tendency and momentum differ enormously, and therefore any attempt to group one hundred cases and decide what has been accomplished is extremely difficult.

I don't know that we pathologists can help you much. I admired Dr. MacCarty's efforts very much, to tell the surgeons, from studies under the microscope, what is going to happen to his patients, and I believe that study will help enormously, but for my part I can't see yet that we get enough data from the microscope to predict with any degree of certainty what is going to happen to the patient, although from time immemorial, pathologists have always known that many lymphocytes and much fibrosis meant local resistance, but how about the extension of the disease, how about the general condition and age of the patient? All of those things are of much wider importance, it seems to me, than the microscopical features obtained from the microscope; so I, myself, have not been able to attribute to Dr. MacCarty's scheme as much importance as others have found in it, and I know of no way in which to determine this course.

That is one of the reasons why I have felt that the conservative methods, especially in operable mammary cases, deserve a much greater trial than they have yet received, and I have perhaps too greatly encouraged Dr. Lee to risk human life by treating some of these mammary cases with radiation. It is being done I find, however, much more widely now than it was five years ago, but you don't find very many reports of it.

I feel also that we don't yet know exactly how best to treat these cases. When I find a tumor of the breast surrounded by lymphocytes and granulation tissue, when I find these histologic signs of resistance in the tissue, I sometimes wonder whether it is wise to put on the roentgen ray and run the risk of destroying this process. There we immediately destroy what many think are Nature's methods of resisting the disease. So I was very much interested in the procedure under those circumstances.

Many think that these cases seem to do well with small doses. Then we have the conflicting reports, namely, of the German sources, as to disastrous results from over-radiation, and from almost identical treatment, reports of good results.

For my part, I don't know of anything which would permit us today to prescribe accurately the proper radiation, and until that can be done, it seems to me that we are very much in the dark as to how best to treat these patients. Another matter which I think might be well worth mentioning before this Society is that in spite of such reports as Dr. Pfahler and the results of Dr. Lee—and I have found they were getting much the same thing in Guy's Hospital in London, and of all the European reports of success, which are now far outnumbering the unfavorable reports—surgeons are not impressed as a whole with the value of radiation treatment of mammary cancer. Dr. Lee didn't tell you that, as a member of the American Surgical Society, he presented this discussion very carefully and successfully in Washington last May, at which time there wasn't a single note of approval from the American Surgical Society. They were practically unanimously against the method, or at least—not to misquote them—they were unquestionably unconvinced of the value of preoperative or postoperative radiation.

So that whatever you are accomplishing, it is perfectly obvious you have not convinced the American surgeons; although a good many of them will submit their cases, you have to

convince the surgical profession as a whole that radiation is of value in surgical cancer. For my part, I think the best way will be to follow the method used in uterine cases, where we first confined our attention to the inoperable cases, to show what could be done, and then went a little further into the more favorable cases, and then finally into the earlier cases which were assigned to the radiologist. That has been done slowly in mammary cancer, but the difficulties are very much greater on account of the great varieties of the disease, and for my part I feel that the most convincing evidence would be a long series of primary operable mammary cancers treated by radiation, either external radiation or, as I believe will be found necessary eventually, interstitial radiation.

It is something that is endless, and I think it is the most important subject that confronts radiology today.

Dr. H. W. Dachtler, Toledo, Ohio. It certainly is difficult to follow such eminent gentlemen in a discussion of this kind, yet, as Dr. Pfahler knows, I have had peculiar opportunity of treating a great many cases of carcinoma of the breast postoperatively. I have had probably better cooperation from the surgeons than the men in the large medical centers.

I think he has talked to some of these surgeons in quite recent years, and he knows that they still feel that there is considerable value in postoperative treatment of carcinoma of the breast.

Personally, I feel that aside from superficial skin lesions, the best work I do is in postoperative treatment of carcinoma of the breast in early cases. I think Dr. Pfahler's statistics and the remarks of Dr. Ewing indicate very definitely that, to be of especial value, we must treat these cases early. There is no difference between carcinoma of the breast or carcinoma in any other location, in that to cure carcinoma, we must get it while it is a local condition. Unfortunately, in most cases, surgeons do not refer their cases without axillary involvement for postoperative treatment, and yet I can't help feeling that that is the most valuable contribution that the radiologist can give at the present time.

I have had something over 300 cases in twenty years. I feel that I can assure a patient that I see, who has no axillary extension at the time of operation, that if she will have an adequate operation, followed by adequate and immediate postoperative treatment, she can be cured of that cancer. I have had a number of cases develop carcinoma of the other breast, eight, ten and twelve years after the primary cancer was treated, but that is not a recurrence. I have seen so few recurrences in that series of cases that I know there is distinct value. Technique is not a matter of discussion in this paper, and yet there is one thing that I must mention in this connection. When I tried a moderate technique and fewer doses, my results were distinctly worse. I have gone back to the treatment of divided doses. We get considerable reaction, but it is a slow reaction. We do not have local recurrence. Of course, the surgeon would say these cases don't recur anyway, but in the early days we saw a great many skin recurrences which probably yielded in a great many cases to radiation treatment, so that we can't help feeling that the surgery fifteen years ago, in the hands of good men, was quite adequate.

I think some of the remarks of Dr. Ewing in the Caldwell Lecture, upon the lymph gland, may be of help here. Perhaps we can advise some of these patients to have purely a local operation and leave the axillary glands. If we can do that, we can get patients to consent to operation much earlier than we do occasionally now.

We may find that we can do the same as I have felt for a number of years about carcinoma of the lower lip. If it has to be done, have the simple excision done and depend upon the roentgen-ray to take care of the glands, not by massive doses.

Dr. Charles L. Martin, Dallas, Texas. I would like to ask Dr. Pfahler a question. My experience is not very extensive, but in cancer of the breast, just as in cancer of the cervix, we have been trying to find out why our patients die, and it seems to me that the findings are rather interesting.

You will remember that I told you a couple of days ago that our cervix cases seemed to die because of broad ligament extension, a thing which is all in the pelvis where you can get at it. So far as we can make out, our treated breast cases are dying, not from anything in or about the chest, but from the things that happen below the diaphragm, and I am almost as worried about the breast case that comes in complaining about rheumatism as I am about the cervix case that complains of pain below the hip, because that is a very common thing. The breast case that comes in, complaining of rheumatism, just like the patient in the cervix case who comes in complaining of pain below the hip, has metastasis. We have autopsied our cervix cases and have found practically nothing in the lungs or the liver or the chest, and yet the bones will be full of malignancy and sometimes the lower spine.

I would like to ask Dr. Pfahler or Dr. Ewing to explain why it is that some of these breast

cases have pain in the hips when you can't demonstrate anything in the bone or spine by roentgen examination; they have very severe pain and limp, and sometimes you can relieve that pain and sometimes you cannot.

I would also like to ask him whether he gives any treatment in the body, below the diaphragm, because it seems to me if we retarded or headed off these metastases, we might lengthen the life of the patient.

In regard to what has been said of good results, I have had in my own experience 3 cases which had a very small nodule in the breast, nothing in the axilla or neck, and literally hundreds of metastases in the whole body, and the patient went on and died. It is these distant metastases, in my experience, which have given me the most trouble. I would like to hear what some of the others think about it.

DR. PFAHLER, closing. I first of all thank Dr. Lee for calling attention to a very evident oversight.

I want to emphasize this fact: That these statistics have been made up of work carried over a period of twenty-five years. If the statistics had been made up from work over the past five or ten years, I believe that the results would show up better. We all know that twenty-five years ago we felt it a triumph if we saw any improvement in any of these cases. Now we feel terribly disappointed when they die or get worse. That in itself indicates that we are making progress. We wouldn't have modified and made our technique what it is today, if we had not felt that the previous technique was not quite so good, but as an estimate of the radiation value in carcinoma of the breast, it seemed better to take this general cross-cut because it probably indicates the value of radiation as used throughout the country, because we will probably find throughout the country all the variations in technique that are involved in this group of cases, and therefore the paper which we have presented probably indicates fairly well the value of radiation as it is today.

I agree with Dr. Ewing that it is most discouraging still. We certainly have much to do. It was so discouraging that when we went over these cases and found "dead, dead, dead, dead," we became so blue over the work that we didn't know whether it was worth-while treating any more cases, but, as you see, when you boil it down and then compare it with other methods we feel that we have made a little progress, that is all. However, there are still many more cases that will be dying. Until we get the majority well, therefore, we must feel discouraged.

I am convinced that the most important thing that any of us—not only radiologists but physicians—can do, so far as our knowledge of cancer is concerned today, is to get hold of the patients for treatment early; make thorough examinations when they come to the physician, and then treat them thoroughly and with the best skill possible. When we do that, we are going to get more patients well. We are fussing about terminal cases. Dr. Martin's question indicates what we are dealing with. When cancer has extended to the liver, I have never gotten one well yet. Therefore, when he asks what to do, while we can delay the process and at least symptomatically the cases have improved, I have never gotten one well in which a carcinoma of the breast had extended to the liver.

I am inclined to agree with Dr. Ewing's interpretation, that these pains in the lower part of the pelvis and spine are probably bone metastasis not yet demonstrable by roentgen rays. If any of you have followed carefully a case that has once extended to the bone, and you have examined the whole osseous system, you will recognize little changes in those bones and in the cortex and in the structure of the cancerous tissue, that would escape your notice if you did not definitely know that you had carcinoma at some part of the osseous system. Yet it may take a long time until that has become clearly demonstrable as a carcinomatous lesion, and that probably explains this group of cases.

I believe that we must help to educate, as Dr. Pirie has indicated, our individual surgeons; convince them that it is of value, and that we can do much by doing our work thoroughly, carefully, conscientiously, and letting the surgeon follow the work that we have done.

THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

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Information of interest to all readers will be found on page i. *Lists of officers of The American Roentgen Ray Society and The American Radium Society will be found below.*

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Twenty-seventh Annual Meeting: Book-Cadillac Hotel, Detroit, Michigan, May 18–21, 1926.

THE AMERICAN RADIUM SOCIETY

President: DOUGLAS QUICK, 350 Park Ave., New York City; *President-Elect:* ALBERT SOILAND, Los Angeles; *First Vice-President:* B. F. SCHREINER, Buffalo; *Second Vice-President:* G. W. GRIER, Pittsburgh; *Secretary:* E. C. ERNST, St. Louis; *Treasurer:* S. M. WITHERS, Denver.

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EDITORIALS

THE INDEX

A new plan has been adopted in regard to the publication of the volume index. Hereafter, instead of appearing in the last number of the volume the index will be published in the first number of the next succeeding volume. That is, the index for the January to June volume will appear in July, and that for July to December in the January number. The reason for this is to avoid the delay in publication of the last number of the volume necessitated by the preparation of the index after the volume is finished. Extra copies of the index will be printed and will be available without charge to those few who may not be continuing their subscriptions.

The work of preparing the index is exacting and time-consuming. The ideal to which we are working and which we are rapidly approaching is to publish in the Journal not only timely original articles but also abstracts of articles bearing, however remotely, on roentgen diagnosis and roentgen and radium therapy. Our index covers not only the original articles but also the abstracts, and is therefore a guide to the world's entire literature on these subjects. Our object is to render a real and increasing service to all who wish to keep themselves informed of the work being accomplished in our specialty in all parts of the world and also to accumulate a reference library of value to those preparing papers or writing books.

In the past there has been from time to time considerable delay in the publication of various numbers of the Journal, and particularly has this been the case with the index numbers. We think that the new plan indicated above will greatly assist us to avoid delay and we hope that it will cause no inconvenience to our readers.

THE ULTRAVIOLET RAY AS A PROPHYLACTIC AGAINST RADIODERMATITIS

A paper by MacKee and Andrews on the above subject was published in the Journal of the American Medical Association in the issue of November 28, 1925. It should set at rest the claims that have been made that the dangers of the occurrence of radiodermatitis can be lessened or entirely obviated by previous ultraviolet radiation.

There never was any rational basis for a belief that exposure of the skin to the ultraviolet ray would render it less susceptible to roentgen injury. There was, in fact, basis for a contrary belief since it was known that the skin effect of roentgen and radium irradiation was often increased by a coincident sunburn.

The experimental work advanced in proof of the contention that ultraviolet therapy is a prophylactic against roentgen-ray or radium injury has never been convincing; the results can probably all be explained by faulty technique or by the fifth conclusion in the summary below

The authors of the paper mentioned above give the following conclusions:

"1. Actinotherapy is of some value in the treatment of chronic ulcers and telangiectasia caused by roentgen rays or radium.

"2. Vigorous actinotherapy, resulting in acute reactions, at or near the time of roentgenization, may enhance the result of the latter.

"3. Tanning of the skin by actinotherapy does not materially increase toleration for roentgen rays or radium.

"4. Preliminary, generalized actinotherapy, even when continued for a long time, does not appear materially to decrease 'radiosensitiveness.'

"5. It is possible to administer several or many times the standard erythema dose of roentgen rays to normal human skin without effecting more than a mild visible reaction. Ignorance of this fact may account for the erroneous assumption that actinotherapy is a prophylactic against roentgen-ray and radium injuries.

"6. It is our opinion that the ultraviolet ray, regardless of how employed, is of no practical value as a prophylactic against acute or chronic radiodermatitis.

"7. It is our opinion that a combination of the ultraviolet ray and the roentgen ray is more likely to be followed by sequelae such as telangiectasia than when the roentgen ray alone is employed."

It is becoming increasingly apparent that the ultraviolet ray has a legitimate place of usefulness in connection with treatment of some conditions that come to the attention of the roentgenologist. It has a definitely benefical effect upon the induration and ulceration due to roentgen injury and lately there have been reports indicating that telangiectasia following radiation can be distinctly improved by its use.

There is no doubt that the use of this agent in legitimate fields will progress more rapidly if false claims such as that mentioned above are set at rest.

JOINT MEETING OF ROENTGEN SOCIETIES

The sections of the American Roentgen Ray Society having been discontinued by action taken at the annual meeting held in Washington, there will be no meeting of the Eastern Section in January at Atlantic City as has been the custom in the past. There will, however, be a joint meeting of the New England, the New York, and the Philadelphia Roentgen Ray Societies at the Hotel Somerset, Boston, on January 29 and 30, 1926. This meeting will be open to all who are interested in roentgenology and radium therapy. Anyone not a member of one of the three societies, who is interested in this meeting, may obtain the program and hotel information by addressing Dr. R. D. Leonard, chairman, Committee on Arrangements, 43 Bay State Road, Boston, Mass.

Subscribers to THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY *visiting New York City, are invited to make the office of* THE JOURNAL *(69 East 59th Street, New York) their headquarters. Mail, packages or bundles may be addressed in our care. Hotel reservations will gladly be made for those advising us in advance; kindly notify us in detail as to requirements and prices. List of operations in New York hospitals on file in our office daily.*

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this column solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES

WE contemplate the publication of a list of roentgen society meetings such as that below, in each issue of the Journal, gradually adding other home and foreign societies as the information reaches us. Secretaries of societies not here listed are requested to send the necessary information to the editor.

NEW YORK ROENTGEN SOCIETY
Secretary, Dr. Eugene V. Powell, 217 East 42d St.
Meets monthly on second Monday, New York Academy of Medicine.

THE CANADIAN RADIOLOGICAL SOCIETY
Secretary, Dr. E. C. Brooks, Montreal.
Meets annually.

ROENTGEN RAY SOCIETY OF CENTRAL PENNSYLVANIA
Secretary, Dr. W. E. Reiley, Clearfield, Penna.
Two meetings a year, April and October.

THE NEW ENGLAND ROENTGEN RAY SOCIETY
Secretary, Dr. Charles W. Blackett, 35 Bay State, Rd., Boston, Mass.
Meets monthly on third Friday, Boston Medical Library.

PHILADELPHIA ROENTGEN RAY SOCIETY
Secretary, Dr. Eugene Pendergrass, University of Pennsylvania, Philadelphia.
Meets monthly on first Thursday evening, Pennsylvania Hospital.,

CHICAGO ROENTGEN SOCIETY
Secretary, Dr. Edward S. Blaine, 2005 S. Wabash Ave.
Meets monthly on second Friday from October to May (except during month of December) at Virginia Hotel. Dinner at 6 P.M., scientific session at 8 P.M.

PACIFIC COAST ROENTGEN RAY SOCIETY
Secretary, Dr. Harold B. Thompson, Seattle, Wash.
Two meetings a year.

CLEVELAND RADIOLOGICAL SOCIETY
Secretary, Dr. E. P. McNamee.
Meetings are held at 6 o'clock at the University Club, on the fourth Monday evening of each month from September to April, inclusive.

CENTRAL ILLINOIS RADIOLOGICAL SOCIETY
Secretary, Dr. C. J. McCullough, Decatur, Illinois.
Regular meetings held quarterly.

SOCIETA ITALIANA RADIOLOGIA MEDICA
Secretary, Professor M. Ponzio, University of Torino, Torino.

THE BRITISH RÖNTGEN SOCIETY
Meets on the first Tuesday of each month from November to June inclusive, at 8.15 P.M., at the British Institute of Radiology, 32 Welbeck St., London; W. 1.

ELECTRO-THERAPEUTIC SECTION OF THE ROYAL SOCIETY OF MEDICINE (CONFINED TO MEDICAL MEMBERS)
Meets on the third Friday of each month during the winter at 8.30 P.M. at the Royal Society of Medcine, 1 Wimpole St., London, W. 1.

BRITISH INSTITUTE OF RADIOLOGY
Secretary, Dr. John Muir, 32 Welbeck St., London, W. 1.
Meets at 32 Welbeck St., but regular dates and times of meeting have not yet been arranged.

SCANDINAVIAN ROENTGEN SOCIETIES
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association. Each of the following societies meets every second month except in the summertime:

SOCIETY OF MEDICAL RADIOLOGY OF SWEDEN
Meets in Stockholm.

SOCIETY OF MEDICAL RADIOLOGY IN NORWAY
Meets in Oslo.

SOCIETY OF MEDICAL RADIOLOGY IN DENMARK
Meets in Copenhagen.

SOCIETY OF MEDICAL RADIOLOGY IN FINLAND
Meets in Helsingfors.

DUTCH SOCIETY OF ELECTROLOGY AND ROENTGENOLOGY
Meets in Amsterdam every second month except in the summertime.

ASSOCIATION OF GERMAN ROENTGENOLOGISTS AND RADIOLOGISTS IN CZECHO-SLOVAKIA
Secretary, Dr. Walter Altschul, German University, Prag, II/52.
Annual Meeting in Prag the last week of October.

THE RADIOLOGICAL SOCIETY OF NORTH AMERICA
Secretary, Robert J. May, St. Luke's Hospital, Cleveland, Ohio.
Annual meeting, New Orleans, La., December, 1926.

SECTION ON RADIOLOGY, AMERICAN MEDICAL ASSOCIATION
Secretary, Dr. M. J. Hubeny, 25 E. Washington St., Chicago, Ill.
Annual meeting, Dallas, Texas, April 19–23, 1926.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION
Secretary, Sherwood Moore, St. Louis, Mo.
Annual meeting, Atlanta, Georgia, Nov. 15–18, 1926.

RADIOLOGICAL SECTION, NEW ZEALAND BRITISH MEDICAL ASSOCIATION

Secretary, Dr. P. C. Fenwick, The Hospital, Christchurch.

Meets annually.

DETROIT ROENTGEN RAY AND RADIUM SOCIETY

Secretary, Dr. Henry L. Ulbrich, 1130 E. Grand Blvd.

Meets monthly on second Friday from October to May, at Wayne County Medical Society Building.

ST. LOUIS ROENTGEN CLUB

Secretary-Treasurer, Dr. L. R. Sante, Metropolitan Building.

Meets first week of each month. Time and place of meetings designated by president.

BELGIAN SOCIETY OF ROENTGENOLOGY

Secretary, Dr. J. Boine, Avenue des Alliés, 134, Louvain (Belgium)

Meets monthly on second Sunday at d'Egmonds Palace, Brussels, except in the summertime.

RADIOLOGICAL SECTION, AUSTRALASIAN MEDICAL CONGRESS

Secretary, Dr. C. A. Anderson, The Hospital, Dunedin.

Meets at Dunedin, New Zealand, during February, 1927.

THE ORAL ADMINISTRATION OF TETRAIODOPHENOLPHTHALEIN

(Editor's Note). We publish below a letter from Dr. Enfield which indicates that the oral administration of tetraiodophenolphthalein for cholecystography has at least one disadvantage that detracts materially from its reliability. The experience of others has shown that a satisfactory shadow of the gall-bladder is often obtained at a second or third examination by the oral method after previous failures. It is also known that many or all of the capsules may remain undissolved even when a common uncoated gelatin capsule is used.

Correspondence is invited on this subject from other readers.

Louisville, Ky.,
November 18, 1925.

The Editor,
The American Journal of Roentgenology and Radium Therapy.

Dear Sir:

For the past few months I have been using orally administered capsules of tetraiodophenolphthalein for gall-bladder visualization.

Early in our experience with these capsules an occasional capsule was noticed unabsorbed and intact in the hepatic flexure of the colon. Since that observation, I have made it a routine to take a film of the entire abdomen as well as of the gall-bladder region at the first examination after the administration of the capsules.

In almost every patient, one or more, and in most instances, several of the capsules have been observed intact in some part of the colon, indicating that at least a part of the dye was not absorbed. In several instances, three or four undissolved capsules have been seen in patients on whom fairly good gall-bladder shadows were obtained.

I wonder if other readers of the Journal have duplicated this experience or if it has occurred to many of them to check up the absorption of the capsules by making a film over the entire abdomen.

I might add that our experience has been perfectly identical with all of three commercially prepared capsules with which we have experimented.

This experience also covers various methods of administration, as for instance, with and without alkali (sodium bicarbonate) administering the capsules all at once or two every fifteen minutes, beginning the administration with the evening meal or at nine o'clock, etc.

Most truly yours,

C. D. ENFIELD.

DEPARTMENT OF TECHNIQUE

Department Editor: DAVID R. BOWEN, M.D., Pennsylvania Hospital, Philadelphia, Pa.

In this department will be published from time to time, as material is available, suggestions for improvement in technique.

A CROSS INDEX IN TERMS OF PATHOLOGY

BY DAVID R. BOWEN, M.D.

Roentgenologist to the Pennsylvania Hospital

PHILADELPHIA, PENNSYLVANIA

AN index system by which the worth while and the unusual may be sifted from the "daily grist" and made easily available for reference has been a besetting and unsolved problem. Conversations with others have afforded much evidence that the writer is not alone in dissatisfaction with the result of many attempts, all of which have proven both irksome as to entry and elusive when their contents are needed.

Some years ago Dr. Manges and the writer began the use of one of the visible index outfits, many of which are now on the market. All have one common feature, i. e., that one line, top or bottom, is used for the title and all the cards so overlapped that this one title line is always exposed to view. Most of these have one inherent defect—that only one side of the card is available for entry and that a considerable part even of that space is taken up by the manner of holding the card in place. A mistake then made was that of letting our plan "just grow." This led to no little difficulty later on when it was found that several titles meaning nearly the same thing had been used.

The present aim is, first, to start with a key list which fairly well covers the range of roentgenological diagnosis and therapy, and is so arranged that any omitted or new title may naturally fit into place.

This key list makes no pretension to be a complete, scientifically arranged list of pathologic entities. The sole aim is to furnish a grouping, with as few units as possible, which will serve as a ready reference to the entire list. Our great troubles heretofore have resulted from a willingness to follow elaborate listings almost to the extent of having a separate card for each and every known unit of pathology. The system here offered greatly reduces the number of cards and, to that extent, simplifies their use.

We make no mention in the key of anatomical groupings. Our method is to use regions and not anatomical units. This is, we believe, so simple that a single illustration will serve without printing the entire list. For instance, fractures of the upper extremity are grouped as those of the shoulder, arm, elbow, forearm, wrist or hand.

Our experience is that this classification groups fractures much more satisfactorily than a listing as bones. A fracture of the olecranon is, for indexing at least, an elbow fracture, its localization in the ulna following logically. A fracture of the radius will be found under elbow, forearm or wrist, according as the fracture is of the head, shaft or base. This manner of classification is followed for all parts of the body.

Of the nineteen main title cards, thirteen are definite pathologic groups; two, UNUSUAL INTEREST and MISCELLANEOUS, are palpably "pigeon holes;" one, DENTAL, is anatomical, and the title PREGNANCY may be either physiological or pathological. The criticism may be made that some of the main groups are too inclusive as, for instance, INJURY or INFECTION. This grouping does, however, have its advantages and we are confident that these advantages will become more apparent as the number of trays necessarily increases. The title OPAQUE MEDIA, to include all opaque material introduced into the body by any method to produce or improve roentgen visibility, is admittedly also open to criticism.

The group UNUSUAL INTEREST has been of real value in having at hand interesting material for the chance visitor, and it holds ultimate promise of excellent teaching material. Naturally, entries under this heading are duplicated on other cards. For instance, a case of carcinoma of the esophagus is entered under NEOPLASM because it belongs there, and under UNUSUAL INTEREST because an esophagobronchial fistula was found. UNDIAGNOSED, under UNUSUAL INTEREST, has also proven of value. The card stimulates continued effort to transfer these entries to appropriate groups with definite diagnoses.

Conditions of questioned or disputed pathology are usually also of rare occurrence and these, properly and conveniently, are entered on the group or main heading card. Should the entries on this card become too diverse they may be posted to appropriate unit cards at any time.

CALCULUS * RENAL

CLASSIFICATION

1 2 3 4 5 6 7 8 9 0

NUMBER	YEAR	PATIENT	SEX	AGE	DOCTOR	L. S.	REMARKS
43633	1925	TOBIN DAVID	M	61	SMITH	✓	MULTIPLE
44006	1925	MANTINO ROCCO	M	37	"	✓	BOTH KIDNEYS Rt. URETER
44231 44296 (CATH)	"	FORAN SARAH	F	29	PERRY		Rt. URETER L LOWER POLE

FIG. 1. Card ruling and sample entries. Listing of doctors' names permits each to readily select his own cases for publication, or other purpose. L. S. when checked (✓) indicates that a lantern slide is on file.

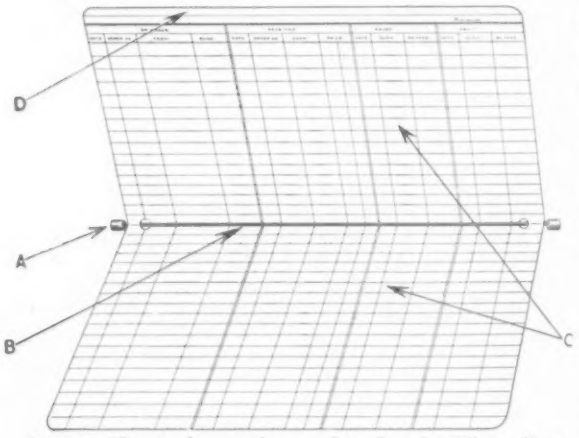

FIG. 2. Illustrating entire card and rod. (The ruling does not refer to this paper.) A. The trunnion that operates in the channel at the side of the panel. B. The spring wire which makes it possible to snap the form in and out of the panel at will. C. This shows two pages of the four-page 4 × 6 form, allowing space for 56 entries, 14 on each page. D. This shows the visible index line. The classification is typed on this line; the individual entries are made in pen and ink.

In many instances it seems well not to follow pathological terminology too minutely. For instance, let neoplasm cover all growths invading or impressing the esophagus, putting the exact name, if known, as, say, carcinoma, in the remarks column. It is not contemplated that every item in the "key" will have its separate unit card; nor does it seem wise to adhere rigidly to a pathological list when, occasionally, an anatomical term may be used to advantage.

For the main group titles red cards are used, for the sub-heads salmon color, and for the unit cards a light buff. The special and miscellaneous are blue.

The ruling is the same in all colors. This ruling (Fig. 1) provides space for repeated numbers in re-examination cases. Inclusion of doctor's name is a necessary aid to the staff member who wishes to sort his own patients from any general group. A check (✓) in the L. S. colomn serves to show that a lantern slide is already on file.

The commercial system chosen has many advantages for this work. All surfaces of a folded card (Fig. 2) are available for entry as handily as the pages of a book, and on each fifty-six separate entries may be made. There is no lost space on the card because of the filing mechanism and the cards may be entered, removed or rear-

ranged with the utmost ease. Various arrangements of trays may be had, differing somewhat in the large but all using the same card and rod device. The double tray illustrated (Fig. 3) holds 150 cards and any multiple of single or double trays may be had, or they may be bought one tray at a time without increasing the aggregate expense.

The advantages claimed are:

1. A definitely planned "key" according to which all entries are made and to which all future amplification may be expected to conform. The attached sample "key" seems very satisfactory in our work and is offered as a suggestion. It can hardly be expected that any other roentgenologist will be able to accept it without some alteration.

2. A visible index plan with a maximum of entries per card and with no waste space. An additional card may even be inserted on the one filing rod, making possible entries under a single indexing space.

3. A minimum of effort in entry and a maximum of ease in reference.

4. Installation cost directly proportional to immediate need in card space.

5. The complete elimination of code lettering or symbols, always a source of confusion, especially if the system must be used by several individuals.

The writer is much indebted to the Postindex Company, of 375 Broadway, Boston, Mass., for assistance in developing this system.

FIG. 3. Illustrating the ease with which forms may be removed or placed in folding panel. The panel, itself, opens and closes like a book. Each panel holds 150 cards, 75 on each side.

KEY LIST

(Used only as a reference or control according to which new cards are initiated. It is also an aid in locating cards in the file, by those unacquainted with it.)

UNUSUAL INTEREST
UNDIAGONSED

CALCULUS
BILIARY
SALIVARY
URINARY

FOREIGN BODY
OPAQUE
NON-OPAQUE
EMPHYSEMA

DEFORMITY
CONGENITAL
absence
anomaly

band
development
  arrested
  prolonged
supernumerary
  (Madelung's, Hirschsprung's etc., etc., if desired)
ACQUIRED CONSTITUTIONAL
ankylosis
bowing
contracture
dilatation
  aneurysm
  ectasia
displacement
diverticulum
fistula
ptosis
ACQUIRED TRAUMATIC
amputation
ankylosis
arthrodesis
pes planus
pseudarthrosis
vertebral
  spondylolisthesis
miscellaneous

INFECTION-INFLAMMATION

ABSCESS
ARTHRITIS
  acute
  atrophic
  hypertrophic
EMPYEMA
MASTOIDITIS
OSTEOMYELITIS
  acute
  chronic active
  chronic healed
  sequestrum
PERIOSTITIS
PNEUMONIA
  bronchial
  lobar
  unresolved
SINUSITIS
  nasal accessory
SYPHILIS
TUBERCULOSIS
  cavitation
  fibrosis
  miliary
  osteitis
  arthritis
ULCER
MYOSITIS OSSIFICANS

INJURY

AVULSION
DISLOCATION
FRACTURE
  epiphyseal separation
  malposition
  malunion
  non-union
  gunshot
GUNSHOT
PUNCTURE OR STAB

OPAQUE MEDIA

CRANIAL
BILIARY
ENEMA
MEAL
SINUS INJECTION
URINARY
  renal
  ureteral
  cystic
VERTEBRAL

NEOPLASM

ADENOMA
CARCINOMA
  metastasis, primary
CYST
EPITHELIOMA
ENDOTHELIOMA
EXOSTOSIS-OSTEOMA
MYELOMA
MYXOMA
NEUROMA
OSTEOCHONDROMA
SARCOMA
  Ewing's tumor
  giant cell
  lympho
  melano
  osteogenic
  round cell
  spindle cell
  osteitis fibrosa
TERATOMA

NEUROSIS

ACROMEGALY
CHARCOT JOINT
GENERAL ATROPHY
OSTEOPOROSIS
ATONY
NUTRITIONAL
  rachitis
  scurvy

OBSTRUCTION

POISONS

PREGNANCY

SCLEROSIS

SEQUELAE

MEDICAL
SURGICAL
TRAUMATIC
MISCELLANEOUS

SPASM

STASIS

TEETH

ABSCESS
CARIES
CYST
FRACTURE
IMPACTION
NON-ERUPTION
PULP STONE
PYORRHEA
ROOT FRAGMENT

MISCELLANEOUS

ATELECTASIS
EDEMA
ENDOCRINE
PERTHES' DISEASE
OSGOOD-SCHLATTER'S DISEASE
SELLA TURCICA

(Most or all of these, doubtless, will be, as others already have been, transferred to other headings.)

A LOCALIZING DEVICE AND PLATE CHANGER FOR MASTOID EXAMINATIONS*

BY G. E. PFAHLER, M.D.

PHILADELPHIA, PENNSYLVANIA

THE greatest possible amount of detail is essential in mastoid films for accurate interpretation. All other things being equal, the smaller the field, or rather the smaller the diaphragm, the greater will be the detail. In order to use a very small field and small diaphragm it is essential that the cone of rays be most accurately directed. Otherwise a part or all of the mastoid area may be missed. In making this statement it is, of course, realized that the mastoid cells may be very extensive in their distribution, requiring a roentgenogram of practically the entire head, or at least all that lies posterior to the sella turcica. Generally, however, a field 3 or 4 inches in diameter will include all of the mastoid cells, and when the rare cases are found, it will be necessary to get the patient back and use a larger field, or to make a large film with the Bucky-Potter diaphragm at the beginning.

The localizer and plate changer which I am describing enables the operator to place the external auditory meatus at an exact point and then to direct the central ray exactly toward this point, or toward any other chosen point in relation to the external auditory meatus.

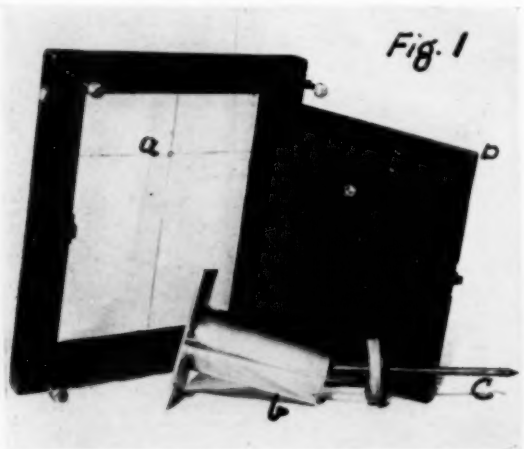

FIG. 1. Shows the cassette holder, or film holder, or plate changer, tilted on end with the door open. The projecting posts are legs upon which this holder stands; *a* marks a small hole in the celluloid films over which the external auditory meatus is placed, or any point that needs to be centered. In the door, *d*, which closes from underneath, directly opposite point *a*, is seen the bulb of a small electric light which projects light directly into this hole and enables one to see from underneath as to whether the meatus is properly centered; *b* is the cylinder attached to the tube stand; *c* is the adjustable pointer which can be lengthened or decreased until it comes directly into contact with point *a* after the proper height has been determined by bringing the cylinder into contact with the head. The pointer is then detached and is removed during the examination.

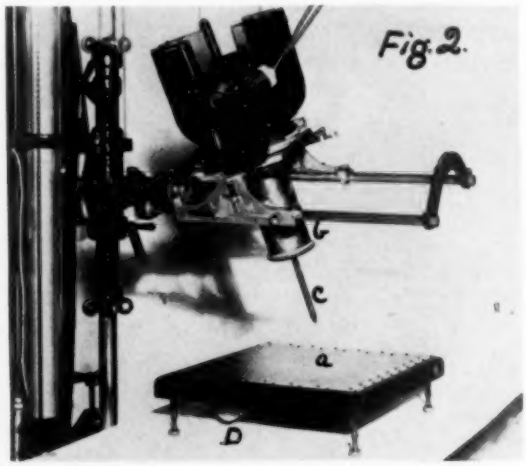

FIG. 2. Shows the head rest in relation to the tube and cylinder; *a* shows the celluloid top of the head rest and plate holder, indicating the point at which the central ray is directed; *b* indicates the cylinder; *c* indicates the pointer; *d* indicates the electric battery which is attached under the head rest.

The plate changer consists of a rectangular frame (14″ × 16″) (Fig. 1), which will exactly fit the largest size 8″ × 10″ cassette, plate holder or envelope, whichever the operator prefers. A piece of celluloid is stretched across this and fastened with brass-headed tacks. It is supported by four rubber-tipped legs (2¾″). The cassette, plate, or film holder is supported by or held up against the celluloid top by means of a door, supported on a hinge. At a point 3 inches from the lower edge of the frame a small ever-ready flash lamp

* Read at the Twenty-sixth Annual Meeting, AMERICAN ROENTGEN RAY SOCIETY, Washington, D. C., Sept. 22–25, 1925; originally shown before the Laryngological Section of the College of Physicians, Philadelphia, Oct. 17, 1923.

is set into this door opposite a dot or hole in the celluloid top over which the external auditory meatus is to be placed. In order to place the patient's head accurately, the lamp is attached to an ever-ready battery controlled by a push button. This light is exactly opposite the dot or hole in the celluloid and with the door dropped one is able to see the meatus as it is brought exactly over this point. Repeated attempts at accuracy without this technique have convinced me that there is no other way (Fig. 1). A localizing pointer is now attached to the cylinder (Fig. 1) to be utilized according to the apparatus in use (Fig. 2). It is my custom to bring the cylinder in contact with the head during the examination. Therefore, to be absolutely accurate, I first of all let the patient lie on the plate changer and determine the position of the cylinder as to thickness of the head. This being noted, I then set the tube holder at this height with the pointer directed toward the small dot or hole in the celluloid, and the angles and positions noted or set on the tube holder. It is my custom to make these examinations stereoscopically; therefore, I note the angle and position for the second exposure with the pointer directed to the dot. The patient's head is then brought into exact position and held by sand bags or head band. The pointer is taken out of the cylinder or swung aside, the cylinder is brought into contact with the head in the position as indicated by the pointer settings and the exposure is made. The tube is shifted without movement of the head for the second stereoscopic exposure. The cassette is turned end for end. A lead number and a lead letter "R" or "L" are placed on the celluloid in advance, which serve as fixed points. The film is then cut for stereoscopic vision. If one chooses to use only a single exposure for each mastoid, the second half of the film can be used for the opposite side. The lead or brass screen for the half of the plate is placed on the celluloid top. This protecting lead cover may be left in place permanently, if one uses this head plate changer only for mastoids, but we use it also for full 8″ × 10″ films of the head. This head plate changer was first suggested to me for general use by Dr. Charles F. Bowen, of Columbus, Ohio.

This description sounds very complicated, but after a few trials the technique becomes almost mechanical. I believe that any technique which increases the precision and the quality of our work is worth while. The device and technique have been of the greatest help to me and my associates.

BOOK REVIEWS

Books Received Are Acknowledged under Heading: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

TUMORS OF THE SPINAL CORD AND THE SYMPTOMS OF IRRIGATION AND COMPRESSION OF THE SPINAL CORD AND NERVE ROOTS: PATHOLOGY, SYMPTOMATOLOGY, DIAGNOSIS AND TREATMENT. By Charles A. Elsberg, M.D., professor of neurological surgery, Columbia University; consultant in neurological surgery, Presbyterian Hospital; attending surgeon, Mount Sinai Hospital, and Neurological Institute, New York City. Cloth. Price, $10.00. Pp. 421, with 354 illustrations. New York: Paul B. Hoeber, Inc., 1925.

In the study of slowly accumulated experiences of the newer fields of medicine, the presentation of cases with their analysis, as used by Elsberg, in his "Tumors of the Spinal Cord" is to be highly recommended.

Cord tumors are rare and no doubt many are missed because of our incomplete knowledge of their symptomatology. The careful analysis of a large group of cases, such as Elsberg presents, will add immeasurably to our information The meticulous care in the preparation of the material and its careful study speaks for the laborious work of the author and his coworkers.

In the chapters on symptomatology, one wonders that the roentgen diagnosis is not given more prominence. Good roentgenography undoubtedly gives valuable information in some extra-dural tumors and in tumors of bony or cartilaginous origin. Though the procedure has not yet been adopted generally by neurological surgeons, the use of opaque media intraspinally with roentgenography is not mentioned nor is the use of air given any space.

The general make-up of the volume, the printing, and the illustrations are admirable and in keeping with the good work usually sent out by the Hoeber press.

"Tumors of the Spinal Cord" will find its way to the shelves of many clinicians as well as of all neurologists and neurological surgeons.

H. H. KERR.

INTERNATIONAL ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN DIAGNOSIS

AMELUNG, WALTHER, AND VON HECKER, HANS. Clinical and roentgenologic observations in hematogenous disseminating pulmonary tuberculosis. *Klin. Wchnschr.*, Jan. 29, 1925, iv, 204–207.

All cases of disseminating pulmonary tuberculosis of hematogenous origin (miliary tuberculosis) are to be considered a single type, despite the variety of clinical pictures and outcome. Although frequently the clinical picture is very mild, sometimes indeed hardly suggesting a pulmonary condition, the roentgen picture clearly reveals an almost uniform seeding throughout the lung area.

The roentgenogram shows a diffuse distribution of more or less closely packed, approximately uniform shadow flakes. In certain lungs the shadows are uniformly distributed, and in others the lateral or lower portions appear to be less involved. The lung apices also are often less involved and one side may show more flakes than the other. These flakes, which are always of approximately the same size and sharply circumscribed appear now well separated, and again running into each other. The dissemination of the single foci and their preference for the central and hilic portions differentiates these forms sharply from those types showing roentgenologically a craniocaudal distribution of the foci. The hilus is usually dense, and glandular swelling is always present. Occasionally one observes lime flakes that are probably Ghon's foci.

BERBERICH, J., AND HIRSCH, S. The roentgenographic representation of the spinal cord (myelography). *Klin. Wchnschr.*, Jan. 1, 1925, iv, 14–16.

Animal experiments demonstrate that strontium bromide serves as a useful contrast substance in the roentgenography of the cord, yielding satisfactory contrasts in the spinal canal. However, the transfer of these attempts to the human have proven unsuccessful because of difficulties in getting a sufficient concentration of the salt into the canal. Iodipin (Merck) was finally selected as most desirable of numerous substances tested on humans. The technique of application is as follows: Lumbar puncture is performed in the lateral position and after measuring the pressure, 5 to 10 c.c. of spinal fluid is run out and under very slight pressure 4 to 6 c.c. of a 10 to 25 per cent solution of iodipin is introduced with a Record syringe. The lateral position is important because this very heavy oil can be introduced only with great pressure if the patient is upright. For this reason it is also advantageous to point the opening of the cannula cranially. Before making a roentgenogram it is necessary to elevate the hips of the patient for a short while. By this technique it is possible to obtain pictures of the whole length of the spinal canal.

Iodipin does not apparently produce any irritation. The administration is not attended by any disagreeable symptoms on the part of the patient. Experience with 20 cases has shown complete absence of paresthesia of the extremities, such as has been observed by Sicard and Forestier after their use of lipiodol. So far as can be determined the iodipin remains in the conus terminalis for months; and clinical studies of the spinal fluid appear to show no alterations due to the presence of the foreign oil.

BIANCHINI, A. Clinical and roentgenological study of diverticula of the bladder. *Arch. di radiol.*, Mar.–Apr., 1925, i, 218–243.

Case histories and roentgenograms are given of 9 cases of diverticulum of the bladder. The anatomy and physiology of the bladder and the clinical symptoms of the condition are discussed in considerable detail. There are various methods of roentgenological examination, such as roentgenography with a contrast fluid in the bladder, roentgenography with opaque sounds, cystoroentgenography in two stages corresponding to the two stages of micturition in diverticulum of the bladder, and cystostereography. The author finds that a much better idea of the condition and of the whole process of micturition is obtained by roentgenoscopic examination with the bladder filled with sterile tepid 20 per cent sodium bromid. This examination shows not only the presence of diverticula, but their number, size, form, site and in some cases their cause, as for example in enlarged prostate. It may also show complications such as tumors or stones in the diverticulum.

BIANCHINI, A. Introduction of oxygen into the scrotum for the diagnosis of diseases of the testicle. *Radiol. med.*, September, 1925, xii, 747–651.

In attempting to inject oxygen into Retzius' space in the course of diagnosis of a tumor of the bladder, the author found to his surprise

that it had not passed into the prevesical space at all but into the scrotum. In searching for an explanation of this fact he decided that, as the patient was quite stout, he had failed to pass the needle into Retzius' space but that it had stopped in front of the transversalis fascia and the gas had passed into the scrotum. He reproduces the roentgenogram which shows the testicles clearly visible in the midst of the oxygen. This gave him the idea of using this method clinically for the diagnosis of diseases of the testicle and epididymis, but so far he has only had an opportunity to try it in one case in which a diagnosis was made of hemorrhagic pachyvaginalitis with atrophy of the testicle. This diagnosis was confirmed by operation. As this is only a single case he presents this as a preliminary note, but he intends to test it further and publish his results. He proposes giving his procedure the name of the pneumovaginal method.

BÜRGER, MAX. Clinical features of hepatic malpositions. *Klin. Wchnschr.*, Jan. 15, 1925, iv, 102–107.

The clinical signs resulting from partial malposition of the liver correspond in many respects with those described by older authors for total hepatoptosis: pain in the hypochondrium varying in intensity with change in position; cough (tussis hepatica) occasionally occurring on assuming an upright position; gastrointestinal symptoms such as vomiting and malaise; attacks of colic suggesting gallstone colic; and peculiar dyspneic symptoms due to the high level assumed by the diaphragm.

Since the introduction of roentgen examination, publications on hepatoptosis have decreased considerably. With better inspection of the topographic variations in the living subject, sharper criteria have been set up than those in the past for the conditions termed hepatoptosis and hepatodystopy. The following groups are distinguished: (1) *Total liver dystopy*. Interposition of foreign organs between liver and diaphragm are included under this term. The condition can occur only if the fixation apparatus, together with the cava as a result of anlage-disturbance, leaves a more or less wide space between liver and diaphragm. Such cases have not yet been certainly demonstrated in the living subject. The anomaly occurring in situs inversus is a spinal case and does not belong under this group.

(2) Under *partial liver dystopy* is understood displacement of the right lobe of the liver such as occurs in spontaneous or artificial pneumothorax, as well as under certain other circumstances.

(3) The term *hepatoptosis* is suggested to describe those conditions in which the liver, together with the fixation apparatus and the diaphragm, moves downward. Two types of this condition may be differentiated: (a) total hepatoptosis occurring as a symptom of general enteroptosis. This has been termed incorrectly by older authors as "wandering liver;" (b) symptomatic hepatoptosis in which the diaphragm, together with the liver is forced downward through rightsided pleuritis, emphysema and pneumothorax.

(4) The last group which, strictly considered, can be assigned neither to liver dystopies nor to hepatoptosis is frequently confused with these conditions and is termed *liver deformation*. The accurate recognition of a large Riedel lobe or of a drawn-out and frequently abnormally movable right lobe due to an enlarged gall-bladder may introduce considerable difficulties from the standpoint of differential diagnosis. Consequently it is apparent that this condition cannot be so sharply differentiated from the above described dystopies and hepatoptosis as we might desire.

BIERMAN, MORRIS I. Chronic appendicitis. Bases for varied clinical manifestations: *Radiology*, August, 1925, v, 152–157.

Clinical experience has shown that chronic appendicitis is frequently masked by what appears to be a chronic gastritis, a cholecystitis, or even a gastric or duodenal ulcer; and intensive study is required to rule out an organic lesion where it is not present. To this end the roentgenographic examination is of great importance. Frequently the first clue to the roentgen diagnosis is that at the six-hour examination, the barium meal is seen to be delayed at the ileocecal valve, and even twenty-four hours after ingestion barium is still to be found in the terminal portion of the ileum. The delay may be due to pericecal adhesions or to spasm of the ileocecal valve and a small portion of the ileum.

When obstruction is due to adhesions, there is practically always found some deformity of the cecum resulting in fixation. The appendix fills and empties at fairly regular intervals, thus showing that although it may be a useless organ it certainly is not a non-functioning one. When a subacutely inflamed appendix has quieted down, or when the condition is chronic, the picture of normal peristalsis in the appendix is modified. Instead of definite regular efficient activity the peristalsis is deficient and the emptying time is extended so that the appendix does not empty itself simultaneously with the cecum. Occasionally an appendix will be found

which contains barium a week or more after the cecum is emptied.

CAMPBELL, WILLIS C. An analysis of bone and joint lesions of known syphilitic origin. *Radiology*, August, 1925, v, 122–131.

A survey is given of 33 cases of bone and joint lesions in which the clinical and roentgenological evidence did not suggest syphilis, but in all of them the Wassermann reaction was strongly positive. The conditions found were infectious arthritis, tuberculous hip, spine, knee, myositis, fractures, ununited fractures, and infectious spondylitis. Seventeen of the cases received intensive treatment, but none showed the slightest beneficial effect of the antisyphilitics. It appears that a Wassermann reaction or a definite history of syphilis does not prove, *per se*, that any particular lesion is syphilitic. It may be that the host harbors more than one disease at a time, as is well demonstrated in the present series of cases.

CARMAN, RUSSELL D. The roentgenologic diagnosis of disease of the gall bladder. *Radiology*, August, 1925, v, 101–103.

Up to September 1, 1924, 178 patients had been examined at the Mayo Clinic by the Graham method. Of these, 39, all with diseased gall-bladders, were operated upon and 34 of them gave abnormal response to the test. In 19 of 25 cases in which stones were present there was no shadow of the dye at any time; in 2 the stones produced a mottling of the shadow; in one there was a faint shadow of the dye at the eighth hour only; in one there was a constant faint shadow, within which was the shadow of a stone, and in 2 the responses were normal. Of 14 cases of cholecystitis without stones there was no shadow of the dye in 8, a shadow visible only at the fifth and eighth hours in 2, and a shadow at the twenty-fourth hour only in one. In 3 cases the responses were normal.

The principle of the Graham method seems fairly well established. The present problem is to make it safe, easy, and routinely applicable, and for this purpose a nontoxic dye has still to be found.

CARRICK, W. M. Pyelography in polycystic disease of the kidneys. *Brit. J. Surg.*, July, 1925, xiii, 75–77.

To show the value of pyelograms in corroborating clinical findings, 2 cases are pictured and briefly described. In the first case the condition existed on both sides, but only the left kidney was injected. The catheter in the right ureter is seen coiled in the kidney pelvis, denoting considerable enlargement. In the second case the opaque sodium iodide solution disclosed a polycystic kidney. Both were female patients, one forty-eight, and the other thirty years old.

CASTORINA, GIUSEPPE. A case of syphilitic osteochondritis. *Pediatria*, March 1, 1925, xxxiii, 265–269.

According to Weill osteochondritis of the long bones is the most typical lesion of hereditary syphilis. It is almost always symmetrical, which distinguishes it from the other diseases which are similar to it clinically, such as fractures and paralysis of obstetrical origin. The roentgenogram is quite characteristic. Normally the juxtaepiphyseal region has a clearly defined linear outline, while in syphilitic osteochondritis it is jagged on account of irregular calcification. According to Wegener there are three stages of the disease: in the first stage the zone of calcification of the cartilage is larger than normal and has an irregular structure. The second stage is characterized by the formation of an intermediate layer between the epiphyseal cartilage and the diaphysis. In the third stage a thick mass with irregular outlines is interposed between the epiphysis and diaphysis which brings about detachment of the epiphysis.

The author describes a typical case in a child two years of age with a syphilitic father. The child was in a poor state of nutrition and could not walk; Wassermann reaction was positive. After a month of mercury inunctions she was in good general condition and the irregularity of calcification of the bones had almost entirely disappeared. The thickening of the periosteum and the curvature of the diaphyses persisted but the child could walk.

COCCHIARARO, GIOVANNI, AND RORDORF, ROBERTO. Suboccipital puncture and the introduction into the spinal canal of substances opaque to roentgen rays. *Riforma med.*, Jan. 12, 1925, xli, 29–32.

American physicians introduced the practice of puncture of the occipito-atlantoid space for the purpose of examining the cerebrospinal fluid in the case of blockade below this point, and Sicard and Forestier conceived the idea of utilizing it for diagnostic purposes by introducing substances opaque to roentgen rays. Lipiodol was adopted for this purpose. This descends in the canal until it is arrested by the pathological process. It was even claimed that the form and nature of a tumor could be determined in this way but a number of cases presented by Martel before the French Surgical Society in 1923, in which the results of operation did not confirm the

findings, destroyed this hope. For whatever the form and size of the tumor the reactive processes caused by it may vary greatly in form, so that the form of the arrested lipiodol may be misleading. It was then tried for the segmental localization of pathological processes and it does, to be sure, serve this purpose, but this can also be accomplished by clinical methods. Madame Sorrel-Déjèrine has reported 18 cases in which there was perfect parallelism between the clinical and lipiodol findings and when the cases improved so that there were no clinical signs of compression the lipiodol was no longer arrested. The author has used the method in 10 cases and gives roentgenograms of 4 of them. He finds that the lipiodol test is not positive any earlier than clinical examination. He believes also that the method is not entirely without danger. In 8 of his cases there was more or less serious disturbance consisting of signs of meningism and aggravation of the symptoms of spinal compression. It is very useful, however, in affections of the cauda equina where diagnosis by other methods is especially difficult. Of course it gives information only as to the site, not the nature, of the tumor. The author thinks the best position for the puncture is with the patient seated and the head flexed rather than the one given by Sicard (lying down with the trunk and head raised).

EGAN, E. "Lipiodol-Lafay," a contrast material for the roentgen examination of the respiratory passages. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, March, 1925, xxxiii, 199–200.

Lipiodol is well adapted for the purpose suggested. This clear, oily fluid is never irritating and appears in certain cases to be of therapeutic use. The technique of use is as follows: After anesthesia of the upper respiratory passage, 15 to 20 c.c. or more of lipiodol are introduced into the larynx by means of a laryngeal syringe. One precaution is essential, the contrast material should be injected into the main bronchus of only *one* side at any single examination.

ENFIELD, CHARLES D. Tetrabromphenolphthalein injection as an office procedure. *Radiology*, August, 1925, v, 104–106.

From an experience with 54 cases, it is concluded that the method of Graham and Cole is successful from the purely roentgenographic standpoint. From the standpoint of diagnosis the principal value of the method is in establishing as normal certain gall-bladders that have been under strong suspicion clinically. At present the principal drawback to the method seems to be the technical complexity of the procedure and the frequency and severity of the reactions. It seems rather doubtful that the present technique will ever come into general use as an office procedure. An ideal substitute would be the same method using a nontoxic dye which could be administered by mouth and which would give equally good shadows.

FRIEDMAN, JOSEPH C., STRAUSS, ALFRED A., AND ARENS, ROBERT A. A clinical radiological study of the gall bladder. *Radiology*, August, 1925, v, 93–100.

An attempt to procure a limited series of particularly well-controlled cases is described in which the internist, surgeon and roentgenologist cooperated. There were three groups of cases. Group 1 was a series of 25 pathological gall-bladders which came to operation and in which distinct gall-bladder pathology was found. Group 2 was a series of 21 normal gall-bladders, all operated on for other causes and in which the gall-bladder at operation appeared normal. Group 3 was a series of 56 normal controls in which no gall-bladder pathology was suspected and which did not come to operation.

The roentgenographic technique involved the use of a spark gap consistent with the patient's thickness, changing the gap at each exposure so that in a series of films the exposures ranged from under- to over-penetration. The most important feature in this connection is the absolute immobilization of the patient's diaphragm.

In the first group of cases a distinct or doubtful gall-bladder shadow was observed in 88 per cent. These were shadows left after the shadows of the bulbus duodeni, pyloric antrum, duodenal arch, etc., shown by the *extra* barium meal film taken in the gall-bladder position had been compared with the gall-bladder films, and eliminated.

In Group 2 only 5 per cent of the cases showed pathological seats, and 14.3 per cent showed stasis. Apparently stasis is almost as frequent in normal gall-bladder cases as pathological. Two of the cases of stasis in this group occurred in patients who showed no gall-bladder shadows. In Group 3 there were found 30.4 per cent positive and doubtful gall-bladder shadows. In one case a distinct gallstone was visible. Stasis was present in only 5.4 per cent of the cases in this group. The data are summarized in tables, and the general conclusion reached is that in pathological gall-bladders verified at operation the diagnostic accuracy of the roentgen ray is 88 per cent. In normal gall-bladders verified at operation the diagnostic accuracy is 85 per cent; and in normal

gall-bladders not verified by operation the accuracy is 75 per cent. Deep gall-bladder seats, wherever found, are an indication of pathology, and stasis is as yet a sign of doubtful value.

GENTILE, NICOLA. Unusual roentgenogram of a foot. *Radiol. med.*, September, 1925, xii, 613–615.

The patient was on a ladder which slipped and he fell on his right foot and had to be assisted to rise. He kept his bed for forty days and was then able to walk only with crutches, and at the end of six months the function of the foot was not restored. Roentgen examination showed two very unusual lesions. The first was a congenital fusion of the second metatarsal with the second cuneiform, and of the third metatarsal with the third cuneiform, while the trauma had caused a scapho-cuneo-cuboid luxation and an astragalo-scaphoid luxation. The mechanism of the injury was a violent supination and adduction. The lower margin of the astragalus was forced against the sustentaculum tali of the calcaneum and the ligaments of the astragalus with the calcaneum and scaphoid lacerated so that the whole foot was displaced inward, leaving the astragalus in normal connection with the bones of the leg; then an excessive supination lacerated the ligaments of the cuboid with the astragalus, the scaphoid and the third cuneiform and an empty space was formed between Chopart's line and Lisfranc's line, into which the head of the astragalus was forced and impacted.

GIONGO, FRANCO. A case of congenital malformation of the pelvis and femur. *Radiol. med.*, August, 1925, xii, 525–535.

The patient was a girl of thirteen who since birth had showed shortening of the right leg and in whom dentition and walking developed very late. At the age of thirteen all the right half of the body is less well developed than the left. There is claudication, vertebral scoliosis, signs of a serious anomaly of the coxofemoral articulation with flattening of the head of the femur, shortening of the distances from the spine of the ilium to the trochanter, from the spine to the pubis, and from the spine to the malleolus, incapacity for abduction and a bony formation in the right true pelvis. Roentgenographic examination showed: scoliosis of the pelvis, ectopy and retardation in ossification of the right acetabulum, hypoplasia of the upper metaphysis of the femur with special adaptation of the head, neck and trochanter.

The author thinks that this is a case of congenital anomaly which may have been caused either by constriction by the amnion or by changes in the layers of the embryo before their differentiation.

HERFARTH, HEINRICH. A peculiar phenomenon in amputation stumps. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, March, 1925, xxxiii, 221–222.

Roentgen examination of old amputation stumps occasionally discloses a band of rarefaction about 1 cm. wide running down the length of the central channel. This was not observed in the corresponding normal limbs nor in recently amputated stumps. Roentgenograms taken in the second plane did not disclose this rarefied band visible in the other plane. A careful examination brought out the fact that this band was produced by the channel of the arteria nutritia.

It appears that this canal becomes visible in the plate after it has atrophied thereby rendering the lamellization and the remaining structures more distinct. Next follows atrophy of the adjacent soft structures; and probably also the artery lying within the channel gradually atrophies owing to disappearance of structures demanding nutrition.

JACKSON, CHEVALIER, AND LEE, WALTER ESTELL. Acute massive collapse of the lungs. *Ann. Surg.*, September, 1925, lxxxii, 364–389.

A discussion is given of the mechanism of acute massive collapse of the lungs and of its relation to foreign bodies in the bronchi and postoperative complications. A few typical cases are described and pictured, and a consideration of various characteristic phenomena leads to the following conclusions:

Acute massive collapse or massive atelectasis is found associated with various conditions. The latter have two factors in common, bearing upon the etiology of pulmonary collapse; namely, embarrassment or paralysis of the respiratory movement, and obstruction of the bronchial tubes. The interference with the respiratory movements may be slight or complete; obstruction has been found to be caused by foreign bodies, bronchial secretion or extrabronchial pressure. Assuming the above two underlying factors, the indications for prophylaxis and treatment of this condition are self-evident. Trauma due to operative procedures must be minimized, and morphine or other inhibitors of the cough reflex should be used conservatively. Fixed or unnatural positions after operation should be avoided and the anesthetic should be of a sort as not to irritate the bronchi; local anesthetics where possible are indicated.

After the massive collapse is established, the dangers are not in the lesion itself, unless

it be bilateral, but in the complications which are apt to ensue. Massive collapse of the lungs is a comparatively rare condition and its incidence postoperatively is approximately 8 per cent. The most characteristic sign is displacement of the heart toward the collapsed lung.

Partial collapse of the lung is probably a very frequent complication following abdominal, particularly upper abdominal operations. In these cases of partial collapse, the arrest of multiple emboli coming from the operative field is probably the mechanism. It is the lesion which so frequently occurs after operations and which is commonly called postoperative or postanesthetic pneumonia. When infection is added to these minute multiple infarctions in the collapsed area a true bronchial pneumonia is established. This is believed to be rather rare as compared with the frequency of partial collapse combined with minute pulmonary embolism and infarction.

KAZNELSON, P., AND REIMANN, F. Results in the roentgenologic demonstration of the gall-bladder with tetrabromphenolphthalein according to the method of Graham-Cole. *Ktin. Wchnschr.*, July 16, 1925, iv, 1390–1395.

The authors have obtained very satisfactory results using the method of Graham in studying the physiology and pathology of the gall-bladder roentgenologically. A total of 30 cases was studied, and in 15 of them where there was no evidence of disease of the liver or gall-bladder the roentgenogram at the eight-hour period showed a visible gall-bladder. The shape of the bladder may be either oval or pear-shaped, lying directly below the shadow of the 12th rib; or in other cases, narrow and long, lying nearer to the vertebrae. In 2 cases of penetrating gastric ulcer the gall-bladder shadow was hook-shaped, probably due to strong adhesions. In 9 cases the gall-bladder could not be visualized and in all of these there was some pathology of the liver or bile ducts.

The experience gained so far indicates that non-appearance of the gall-bladder shadow after eight hours is indicative of pathological condition. On the other hand, presence of the shadow does not always indicate a healthy condition, although it usually does. In 6 cases the gall-bladder was visible, although disease of the bile duct was present.

With this method of visualization of the gall-bladder available, an attempt was made to observe the action of the well-known Witte peptone reflex. It was found that after injection of oil by means of a duodenal sound there occurred a prompt contraction of the gall-bladder shadow to less than half its original size. The effect of pituitrin was likewise tested. In this case there resulted a change in shape of the gall-bladder apparently in the sense of a pronounced increase in tone of the bladder wall. In another case the antagonistic action of atropin to the pituitrin-contracted gall-bladder could be demonstrated.

LAPENNA, MARINO. Roentgenological study of tumors of the colon. *Arch. di radiol.*, Mar.–Apr., 1925, i, 264.

Six cases are described and roentgenograms given, one of sarcoma of the mesocolon partially infiltrating the wall of the intestine, one of cancer of the upper third of the ascending colon, one of cancer of the cecum, one of tumor of the middle third of the descending colon, one of perforating tumor of the left flexure and the other of tuberculoma of the cecum involving also the last loop of the ileum. Characteristic roentgenological signs of all tumors of the colon are stenosis, incontinence (rapid passage) and deformity of the affected tract. In some cases the obstruction is suddenly overcome and the barium passes beyond the tumor, particularly in beginning stenosis. This was noticeably true in the first case of extrinsic tumor, and another characteristic feature of this case was that the wall of the intestine seemed to be pulled over toward the wall of the abdomen and adherent. In examination with a barium enema sometimes deformities of the intestine, especially the descending colon, are observed which are spastic in nature and not due to the organic lesion. Two of the roentgenograms show the differences between spastic and organic lesions. The sixth case is interesting because it is unusual to observe such an intense stenosis from a cecal tuberculoma. It was as extreme as that usually seen in new growths of the colon.

KURTZAHN AND WOELKE. Contrast substances in the air passages. *Fortschr. a. d. Geb. d, Röntgenstrahlen*, March, 1925, xxxiii, 215–221.

Experiments on dogs and occasional observations on man show that the bronchi of man and dog are surprisingly little sensitive to barium sulphate suspensions and oil suspensions of contrast substances. The occasional pneumonias observed after entry of contrast materials used in the roentgen examination of perforating esophageal cancers appear to be due not alone to the shadow-producing material but also to the aspiration of fragments of food and brokendown tumor tissue. The entrance

of small quantities of sterile contrast suspension into the bronchi is apparently not very dangerous in an individual with healthy lungs.

This method often furnishes a clear picture of the shape of the bronchi, bronchial fistulas, and bronchiectasis. A filling sufficient to enable diagnosis of all portions of the lung is obtained only with relatively large quantities of contrast suspensions (in case of a medium-sized dog, about 50 c.c.). A corresponding amount in the air passages of the human is not to be thought of. It is conceivable that one side may be thus filled while the other lung remains functioning normally; and this makes it possible to get an idea as to the changes in the lung itself by roentgenologic outline of the bronchial tree. There is no information that would indicate this method to be without danger in the case of individuals with affected lungs.

A careful roentgenoscopic examination of the patient and a technically perfect roentgen picture, together with a stereoscopic examination without employing contrast substances, all enable the clinician as a rule to recognize and localize a disease process in the pulmonary regions. In addition there are of course the customary clinical methods of examination, so that there appears to be no justification whatever for the procedure involving insufflation of contrast material into a sick lung merely for purposes of obtaining "interesting" roentgenograms.

MEYERDING, HENRY W. Multiple myeloma. *Radiology*, August, 1925, v, 132–146.

Not infrequently the roentgenogram gives the first information as to the true nature of multiple myeloma, and no doubt it is largely responsible for the increased number of case reports finding their way into the literature. Especially important is the ability of the roentgenologist to determine the local or general character of the neoplasm; and pulmonary metastasis is demonstrable in the roentgenogram long before clinical signs appear. The tumor may be so extensive as to make differentiation difficult or impossible, the whole bony structure being replaced by tumor tissue thus producing indefinite shadows in the roentgenogram. The etiology of the condition remains unknown; of the 13 cases which are briefly described and discussed, a history of trauma was given in 6, infection in 4, and trauma plus infection in one.

The prognosis of these cases is unfavorable. The average length of life in the present series was approximately twenty-two months from the onset of symptoms, the shortest duration was three months and the longest fifty months. In treatment roentgen therapy should be given a trial. Transfusion has been resorted to but is of transient value.

NASSA, VINCENZO. Contribution to the roentgenological diagnosis of Barlow's disease or infantile scorbutus. *Radiol. med.*, September, 1925, xii, 624–636.

In 15 cases of Barlow's disease the author studied the roentgenological signs of F. Fränkel and H. Wimberger. The former consists of a shadow at the diaphyso-epiphyseal line at the distal end of the femur and the proximal end of the tibia, or it may be found only at the distal end of the femurs, or even only one of them; it is more or less intense, irregular, denser in the center and decreasing toward the sides, directed transversely and found at the so-called "zone of detritus." If it is found in both tibias and femurs it is called a total sign, and if only in the femurs or one of them it is called a partial sign. Wimberger's sign consists of a border of denser bone at the periphery of the epiphyseal centers of ossification, especially of the femurs.

Among his 15 cases the author found Fränkel's sign in 13, five times total and 8 time partial; in 6 cases he found Wimberger's sign markedly positive, in 2 uncertain, in 7 clearly negative; in 2 cases, and in the same subjects, both the signs were negative.

From control examinations made in 20 cases of florid rickets, 3 cases of acute poliomyelitis in the phase of stabilization of the paralysis in subjects at least two years old, a case of congenital myxedema in an infant nine months of age, a case of hypoplastic constitution in a subject at least two years of age and 3 cases of congenital syphilis, and in view also of the fact that all the 15 cases of Barlow's disease were accompanied by rickets, the author comes to the following conclusions:

(1) The most constant sign is that of Fränkel, which is also the most specific since it has an anatomical substrate, the zone of detritus of Schoedel and Nauwerck.

(2) Manifest clinical and roentgenological signs of rickets are necessary in order to produce Wimberger's sign.

(3) Wimberger's sign may be interpreted as being due to central decalcification of the bone of rachitic origin, which brings about an apparent condensation at the periphery of the center of ossification. It is not a specific and pathognomonic sign of Barlow's disease alone, but only of Barlow's disease associated with manifest rickets. Yet Wimberger's sign should be looked for in all certain and suspected cases of Barlow's disease, though it does not have the definite diagnostic value of the more con-

stant, more characteristic and more specific sign of Fränkel.

(4) Wimberger's sign is not found exclusively in scorbutus in nursing infants but also in children somewhat older. The author describes one case in a child three years and eight months old.

NICHOLS, BERNARD H. Differential diagnosis of gallstones and kidney stones. *Radiology*, August, 1925, v, 107–121.

In a fairly large percentage of cases calculi cannot be identified by the size, shape or general appearance of their shadows and in such cases specific means of differential diagnosis are required. Of greatest value is the use of the anteroposterior and posteroanterior exposures in accordance with the principle used in localizing foreign bodies. In general, when the shadow of the stone on the posteroanterior or gall-bladder film is smaller in size, more distinct in outline, lower in position and nearer the vertebral column than the shadow of the same stone in the anteroposterior or kidney film, the diagnosis of a gallstone may safely be made.

A valuable auxiliary measure is the examination of pyelograms after the injection of full strength sodium iodide solution which, in the case of kidney calculus, will locate the shadow in the pelvis of the kidney; or of a 5 per cent solution by means of which the kidney pelvis can be well outlined, and the calculus can be seen on the pyelogram in the pelvis or calyx of the kidney. In the case of a gallstone, the shadow in the pyelogram will almost always lie outside the kidney pelvis. Important also for differential diagnosis are careful roentgenographic studies of the pyloric end of the stomach, of the duodenum and of the hepatic flexure for direct or indirect evidence of gall-bladder disease.

PAZZI, ERMANNO. Change in the technique ordinarily used in making a longitudinal roentgenogram of the tuberosity of the calcaneum. *Arch. di radiol.*, Jan.–Feb., 1925, i, 14–16.

Axial fractures of the tuberosity of the calcaneum sometimes do not show in lateral pictures. To take a longitudinal picture Holzknecht advises having the patient stand with his foot on the plate with the leg running obliquely forward and the knee flexed so as to expose the calcaneum as much as possible. This gives a good picture but the position cannot be assumed by a patient with fracture or severe contusion. The patient should be laid on the table in ventral decubitus with the tip of the foot touching the table at right angles with the leg; the plate is stood against the sole of his foot and immobilized with sandbags and the tube inclined to the calcaneum as in Holzknecht's position. Or if the picture cannot be taken in this position because of tremor or for any other cause the foot may be allowed to hang over the edge of the table, the plate laid against the sole and held in position with one of the supports in ordinary use in roentgen rooms.

In this way a good axial projection of the tuberosity can be obtained, although a little deformed from being elongated. Plates are given showing two cases of axial fracture of the tuberosity of the calcaneum in lateral and longitudinal projections.

PAZZI, ERMANNO. Calcified glands in renal tuberculosis. *Radiol. med.*, August, 1925, xii, 536–542.

Two cases of tuberculosis of the kidney are described in which roentgen examination showed shadows which in the first case appeared to be a calculus in the kidney pelvis and in the second in the ureter. The author suspected that they might be calcified glands but was unable to prove it by roentgen examination, so nephrectomy was performed in both cases as it was indicated by the kidney condition. After the operation the shadow remained in both cases, a little displaced downward due to the changes in the position of the tissues affected by the operation. In both cases the shadows were evidently caused by calcified retroperitoneal glands. A third case is described in a patient of twenty-eight, with a family history of tuberculosis who had always had indefinite abdominal disease and recently had had hematuria. Roentgen examination showed a shadow apparently in the course of the ureter at the level of the transverse process of the third lumbar vertebra. But on pressure on the abdomen it could be displaced to the front of the spinal column, showing that it was outside the lumen of the ureter. Because of its free mobility it was assumed to be a calcified gland of the mesentery.

The author has found few cases like the first two in the literature but thinks that they are probably more frequent than would be indicated by the reports.

PAZZI, ERMANNO. Sinusitis of the right maxillary sinus caused by a second molar tooth. *Arch. di radiol.*, Mar.–Apr., 1925, i, 244–247.

A peasant woman of sixty-five came for treatment of a fistula of the right cheek. She gave a history of having fallen on a stone in the fields three years before. There was a

lacerated contused wound of the right cheek which healed in a little while; there was no bleeding from the mouth and she could eat without difficulty. After some months an abscess of the cheek developed which left a fistula. Roentgenograms in the anteroposterior and lateral directions showed an opacity of the right maxillary and ethmoid sinuses which was identified as a second molar tooth, completely developed. The author thinks this was a supernumerary tooth retained in the sinus and not a second molar that had been pushed in by the accident because the patient reported that she had had no bleeding of the mouth at the time of the accident, not much pain and that she had lost no tooth at that time. She had lost many of her teeth from caries. Moreover the tooth showed no erosions indicating that it had been used and its position was that of a tooth which had developed in a normal direction, not that of one that had been pushed into the sinus. There were other anomalies of the teeth in this patient, including retention of the third molar of the right side in the mandible and deviation of the second premolar of the same side, which was almost retained in the rarefied alveolus.

Cases of this kind are extremely rare. Supernumerary teeth retained in the nasal cavity are more frequent. Some cases have been reported of teeth retained in the maxillary sinus but they were not fully developed and in the few cases in which they were molars they were always the third molar, the wisdom tooth.

PIERGROSSI, LAMBERTO. Contribution to the roentgenology of abdominal tumors. *Arcb. di radiol.*, Jan.–Feb., 1925, i, 16–51.

The author describes in considerable detail the passage of the barium meal through the normal gastrointestinal tract and gives brief notes of a number of cases of tumor. He discusses the differential diagnosis between intrinsic and extrinsic tumors of the digestive tract and emphasizes the falciform outline of the former. Perhaps the most valuable part of the work is six plates showing 51 roentgenograms of the normal gastrointestinal tract and of his tumor cases.

PIERGROSSI, LAMBERTO. Painful affections of the colon. *Arcb. di radiol.*, Mar.–Apr., 1925, i, 264–328.

Formerly almost any complaint of pain in the right iliac fossa accompanied by a feeling of heaviness and pulling and by constipation was diagnosed appendicitis, acute or chronic, and appendectomy performed. But many of the appendices removed in this way were found practically normal. Later Lane gave the name of chronic intestinal stasis to some of these cases, emphasizing the symptom of constipation, but in some cases there is an alternation of constipation and diarrhea. Donati gave the name of ileo-colic stenosis from abnormal position to the majority of these affections. This is more exact than Lane's name but in many of the cases it is not a true stenosis in the ordinary sense of the word, but merely an interference with intestinal circulation from the mal-position of the ileo-colic loop and colon. The author adopts the general name of painful affections of the colon for these conditions and mentions the many causes to which they may be due, including congenital abnormalities of form and position of the colon such as Jackson's pericolic membrane, total or partial dolichocolon, congenital and acquired megacolon, high position of the cecum, mobile cecum, acquired abnormalities of position, such as ptosis of the cecum, gastro-colic ptosis, prolapse of the colon, double N bend of the colon in the right flank and abnormalities of position due to inflammatory adhesions, such as Lane's kink, adhesion of the ileo-colic loop to the cecum and insufficiency of the ileo-cecal valve and double gun-barrel adhesions of the flexures of the colon.

He discusses the literature of these conditions, gives an extensive bibliography, and 28 roentgenograms.

PORRO, NICOLO. Roentgen study of ectopy of the teeth. *Radiol. med.*, August, 1925, xii, 543–546.

Among the different forms of ectopy of the teeth those which are most interesting from the point of view of stomatology are those due to migration of the follicles in which one tooth may develop outside its normal place and at a great distance from it. It may develop at any place in the cranium but most frequently in the sinuses.

Roentgen examination, by which these structures may now be studied, has shown that the ectopic teeth may develop in the maxillary frontal or even the spenoid sinuses.

The author reports the case of a man of forty-two, who for some years had shown a swelling of the malar region, which was accompanied by periodical attacks of pain which were at first thought to be due to chronic maxillary sinusitis. But it was finally shown by roentgen examination that these attacks were caused by the presence of a large molar tooth which had developed in the antrum of Highmore. The author from the results of his own examinations and similar ones described in

recent years in the literature concludes that when certain syndromes suspicious of sinusitis or maxillary neoplasms are found a roentgen examination should always be made before performing any sort of operation.

SCADUTO, G. Congenital absence of the head and neck of the femur. *Arch. di radiol.*, Jan.–Feb., 1925, i, 11–14.

A child of five had had a slight limp since she began to walk and her body inclined somewhat to the right. One physician had made a diagnosis of luxation of the upper epiphysis of the femur and another had said she was suffering from a badly healed fracture of the coxo-femoral joint and advised operation. As the parents were unwilling, in view of her symptoms, to have her subjected to operation they brought her to the author for roentgen examination, which showed complete absence of the head and neck of the right femur. In 1919 he saw a similar case in a man of thirty-four. He believes that these cases are ones of congenital deformity and are not due to deforming osteochondritis as has sometimes been claimed. Roentgen examination is very essential as it may save the patient from operation on a mistaken diagnosis.

SPIESS, GUSTAV. The value of roentgen examination in demonstrating and following the clinical course of foreign bodies in the gullet. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, March, 1925, xxxiii, 236–238.

If the foreign body is not too small roentgenoscopy is to be preferred as a diagnostic aid; and in the case of very small objects the roentgenogram is the more useful. If the object is not discovered on the plate it is no sign that it has disappeared. Frequently the consistency or density is such as not to throw a shadow. In that event serial roentgenograms should be taken or else a direct endoscopy performed.

SHORT, A. RENDLE. Case of von Recklinghausen's osteitis fibrosa. *Brit. J. Surg.*, July, 1925, xiii, 170–174.

A case is described occurring in a woman, aged forty-six, dating from childhood and perhaps from birth. Many bones were involved, but until recently there were no symptoms. The tibia shows bone erosion and expansion. The femur shows a mixture of bone erosion and new bone formation within the shell of the cortex. The marrow has been converted into fibrous and myxomatous material, and shows in places many proliferated cells, probably endosteal in origin. The thick layer of very porous bone seen in osteitis deformans is not present.

The case is peculiar in the following respects: It occurred in association with many subcutaneous nevo-fibromas; fractures were absent; the knee joint was swollen and gave great pain; in the sections examined osteoclasts were very scarce; rods and pearls of osseomucin were present in the region which should have been occupied by bone marrow, thus resembling cartilage to the naked eye.

SIELMANN, RICHARD, AND SCHINDLER, RUDOLF. On the roentgen and clinical diagnosis of polyposis ventriculi diffusa. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, March, 1925, xxxiii, 191–195.

The diagnosis of this condition should first be attempted by means of careful roentgenography, and when this procedure fails a gastroscopic examination should be undertaken. Certainly, an operation should not be attempted until adequate visualization has been secured. Because of the frequency of polyps they should be taken into consideration in cases of achylia with hemorrhage, and in achylia with excessive production of mucus. A detailed description is given of a case occurring in a woman, aged thirty-one. The roentgen examination showed the stomach in normal position with active peristalsis, good tonus and a small air bubble. The greater curvature had a toothed appearance, especially near the pylorus. The bulbus duodeni also failed to show a smooth outline. The characteristic behavior of a contrast meal left a strong suspicion of polyposis and this was confirmed gastroscopically.

VOGL, ALFRED. A case of penetrating gastric ulcer and epiphrenal esophagus diverticulum. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, March, 1925, xxxiii, 196–199.

A report is given of a case occurring in a man, aged sixty, which was studied both roentgenologically and at postmortem. Roentgen observation showed in the filling of the esophagus with barium that the contrast material first flowed into a sac about 3 cm. above the cardia, rested for a moment after filling the sac and then pushed upward past the diverticulum into the stomach. The pouch had all the characteristics of a pulsion diverticulum. There was a niche in the smaller curvature of the stomach which taken in connection with a local hourglass spasm and the occurrence of occult bleeding pointed to the presence of an ulcer penetrating into the pancreas. At autopsy the diverticulum was found exactly as expected. The simultaneous occurrence of diverticulum and penetrating ulcer are believed to be merely accidental.

ZORZI, PIETRO. Etiology of dolichocolon. *Radiol. med.*, August, 1925, xii, 547–555.

From a roentgenological study of dolichocolon Zorzi believes that these anomalies are not congenital, at least in the majority of cases. On the contrary there are very important arguments, clinical, roentgenological and therapeutic, to indicate that they are acquired.

Clinically dolichocolon may present no symptoms, though this is rare; more frequently the symptoms are those of colitis. The most violent symptoms are not due to the dolichocolon itself but to some complication, such as volvulus, occlusion, pelvic peritonitis, megalocolon, etc. This clinical conclusion is confirmed by roentgen examination. Dolichocolon has the same segmental tendency as constipation and colitis. Just as there is a right and a left variety of constipation and colitis, dolichocolon may be classified into two great classes, the proximal and the distal. There is nothing to show that it is the dolichocolon which causes the constipation and the colitis, and not the latter which cause the former. And a third hypothesis is possible, namely, that there is no causal relation between the constipation, the colitis and the dolichocolon, and that all three form a syndrome caused by a change in function of the extrinsic nerve plexus of the intestine. The segmental tendency of the lesions seems to confirm this interpretation.

By repeating the roentgen examinations at long intervals it is possible sometimes to find a colon of normal length or almost so in the same subject who had formerly had a dolichocolon. Or better still, a dolichocolon may be cured by the use of diathermia.

The author believes that considerable variations in length may be produced in the large intestine as a result of different conditions, such as capacity for adaptation of the intestinal walls to chemical variations in the feces, endocrine changes in the sympathetic and autonomous nervous systems, inflammatory changes in the sensory apparatus of the mucous membrane, toxic impregnation of the abdominal plexuses, etc. The extent of these elongations varies, depending on the persistence of these conditions and whether more than one of them coexist.

ROENTGEN AND RADIUM THERAPY

CRAMER, H., AND KALKBRENNER, H. The treatment of inflammations with roentgen rays. *Klin. Wchnschr.*, May 21, 1925, iv, 1019–1022.

A surface dose of 20 per cent of the skin unit dose produces an undoubtedly favorable effect upon an inflammatory process. Acute inflammations are more amenable to irradiation than are chronic processes; indeed, some of the latter appear to be refractory to the radiation. The early phase of an inflammation seems to be the best time for administering roentgen rays; the peak of the inflammatory process seems to be a less favorable time.

The favorable effect of the roentgen therapy consists, mainly in the amelioration of pain, relief of the general symptoms and shortened duration of the inflammation. Surgical treatment of inflammation is successfully supported by combination with roentgen irradiation. Here, too, the healing process is much accelerated as compared with purely surgical treatment.

Any explanation as to the mechanism whereby roentgen rays act upon inflamed tissue will have to be sought in the stimulation of some physiological defense apparatus to an increased activity. This is a complex matter, none of the details of which seem to be very definitely visualized.

FARRAR, LILLIAN K. P. Preliminary report of primary carcinoma of the cervix treated with radium in the Woman's Hospital in the State of New York. *Am. J. Obst. & Gynec.*, August, 1925, x, 205–213.

The three-year end results of primary carcinoma of the cervix treated with radium show in the group of operable cases 23 alive out of 31 cases traced, and in the group of inoperable cases 35 alive out of 102 cases traced.

The initial dose of radium has been 100 mg. in one tube placed within the cervix for twenty-four hours, together with needles if involvement of the vagina, bladder or rectum is present. In women under thirty, in whom cancer cells are more resistant, the dose has been 100 mg. for thirty to thirty-six hours. This is merely a therapeutic or test dose, and the results obtained have been a guide for subsequent treatments. Each case is a study in itself and there is no uniform dose in the successful treatment of cancer. The successful result depends not only upon the direct killing of cancer cells, but also upon a cicatrization of the cervix and occlusion of the blood vessels.

If at the end of eight weeks from the first radium treatment a pale cicatrix has not formed or healing is not definitely progressing in the cervix, a second radium treatment is given, the dosage depending upon the response to the first dose. Repeated doses may be necessary to arrest the tumor cells persisting in the scar. Since results of radium treatment depend also upon the defense reaction of the

body and tissues, every effort should be made to secure for the patient a favorable environment following the treatment. Blood transfusions have been found especially advantageous in assisting the body defenses.

FINZI, N. S. Some developments in deep radio-therapy. *Brit. J. Radiol.*, April, 1925, xxi, 67–79.

Deep roentgen-ray therapy in Great Britain is still behind progress in Europe as a whole, but it is hoped that this disparity will not persist for long.

A general description is given of some of the modifications in technique at present in use. Present day practice employs three general methods of roentgen therapy: (1) multiple short distance fields; (2) few long distance fields, and (3) one or two long distance fields with a number of accessory short distance fields.

In the treatment of carcinoma of the breast the author has devised a method called the "skimming" method to avoid injury to the lung parenchyma. The method is designed to give a full carcinoma dose to the tumor. A block of wax is placed on the skin in order to obtain a homogeneous scattering medium and the dose of rays is applied at a tangent to the ribs, with the tube far enough away—50 cm. is sufficient with a penetrating radiation. In this manner only a small portion of the surface of the lung will be reached by the radiation.

GUARINI, CARLO. Radiological treatment of chronic tonsillitis and hypertrophy of the tonsils. *Riforma med.*, March 16, 1925, xli, 252.

Radiological treatment of the tonsils was introduced in 1913 by Nogier and Regaud. Since then it has been adopted by many physicians, especially Americans. Either radium or roentgen rays may be used. Berven Elin has treated 154 patients with radium, using an apparatus which he himself devised for fixing the radium on the tonsil. The radium is left in place two to three hours; each tonsil is treated once, and the interval between the treatment of the two tonsils is four to five weeks. He had improvement in 135 cases. Witherbee reports the technique for roentgen treatment. The patient is laid on his back and turned on the side to be treated. The central ray of the tube is directed so as to pass immediately behind the mandible, encountering the tonsil and rhinopharynx. Each treatment lasts four to five minutes. The field to be irradiated measures 7.5 × 6.5 cm.

The best results are obtained in true soft hypertrophy in childhood. In hard hypertrophy in adults where there is more or less sclerosis of the tissue the results are not so good. In general, the results are very satisfactory. Within two weeks the volume of the tonsil decreases, the hyperemic color disappears and the tonsil becomes smooth and rose-colored. The caseous matter is discharged from the crypts. The pain and difficulty in swallowing also disappear and the general health quickly becomes normal.

The advantage of radiotherapy is that it is simple and painless and avoids operation. Radium treatment has the disadvantage that it is unpleasant because the patient must wear an apparatus which keeps the mouth open for rather long periods of time. Williams says that radium is preferable because the irradiation is more constant and it is easier to control the dosage. The author prefers roentgen rays because with present methods and apparatus the dosage can be accurately controlled. He reserves radium for cases in which immobility of the patient cannot be obtained, as in small children.

D'ISTRIA, ANTONIO. The treatment of anterior poliomyelitis. *Arch. di radiol.*, Jan.–Feb., 1925, i, 66–75.

The histories are given of 15 cases of children all suffering from paralyses of the lower limbs as a result of anterior poliomyelitis. The paralyses varied in extent, they had persisted for from ten days to thirteen months and in all cases there was improvement in the motor deficiency and the trophic changes after roentgen irradiation combined with galvanization over the lumbar spinal column. All the children were given several series of irradiations at intervals of one to two months, four or five treatments and ½ to ⅔ erythema dose being given to a series with very hard rays. The patients at the hospital for incurables were treated with a Corbino and Trabacchi apparatus, intensive model, Coolidge tube, spark gap 32 cm., skin distance 30 cm., intensity 2 ma., filter 1 mm. aluminum and 0.5 mm. zinc; private patients with a Symmetril apparatus of Reiniger, Gebbert and Schall with 35 cm. spark gap, Coolidge tube, skin distance 35 cm., intensity 2 ma., filter 0.5 mm. zinc and 1 mm. aluminum. The ray was centered on the 12th dorsal vertebra without any inclination of the tube, and a diaphragm 9 cm. in diameter used. The author does not agree with Bordier in trying to limit the irradiation to a very small field as this is difficult or impossible anyway in restless children and with the large field he obtains a larger deep dose.

The results are much better than those obtained with electrical treatment alone

(spinal galvanization, hydroelectric baths, galvanization of individual muscles); the results have also been much more prompt since the roentgen treatment has been adopted.

The author believes that the effect of the roentgen rays is due to their destructive action on all tissue extraneous to nerve tissue in the anterior horns. The rays do not have any effect on nerve cells and fibers but they destroy all tissue which remains as a result of the inflammation. They destroy infiltrations and vascular proliferations, and exudates are absorbed without becoming organized and they particularly destroy the young connective tissue which would otherwise infiltrate between the nerve cells and fibers in the focus of inflammation and would later retract and cicatrize and crush out the nerve tissue. The object of roentgen treatment is to save from such destruction all nerve elements that have not already been destroyed by the inflammation. If the treatment is given in time the young connective tissue is destroyed and the nerve cells saved from being crushed by it; the nutrition of the cells which remain is improved and the circulation in the gray nuclei of the spinal cord is improved.

No bad effects were observed from the treatment. Sometimes after the first irradiation the children had nausea and vomiting, but this was always transitory and did not appear after the other irradiations.

HOLFELDER, HANS. Concerning the limits of deep *x*-ray therapy and operation in the treatment of malignant growths. *J. Cancer, Dublin*, April, 1924, i, 61–80.

Roentgen rays will effect a successful cure only where it is possible to confine them locally to the diseased part. It is therefore the aim to manipulate roentgen rays just as precisely as the surgeon's knife or cautery. In other words, the art and skill of the roentgen-ray specialist are decisive.

There are a great many very heroic and technically very skillfully worked out cancer operations in which the operation is formidable, and the success obtained very little. In roentgen therapy we have a means which in these particular cases is able to do the same if not much better than operation. Experience with mammary carcinoma indicates that cancer in Stage I of Steinthal should undergo thorough surgical treatment at the earliest possible moment. Even in Stage II operation is superior to roentgen treatment. Stage III has an absolutely bad prognosis from operation, but prophylactic after-treatment with roentgen rays has shown some very favorable results.

The fields in which deep roentgen therapy are applicable are gradually being extended and cultivated, but successful results are still infrequent and irregular. The results of roentgen therapy can never be predicted in advance; on the other hand, the surgeon is in a position by reason of findings at operation to give the patient a probable diagnosis. The reaction of cancer to roentgen rays cannot, however, be calculated. In those regions where operative surgery itself is not satisfied with its results roentgen therapy is today able to replace and compete with the knife with a good chance of success.

LEE, BURTON J., AND HERENDEEN, RALPH E. An evaluation of preoperative and postoperative radiation in the treatment of mammary carcinoma. *Ann. Surg.*, September, 1925, lxxxii, 404–412.

A comparative study is presented of the results obtained in a series of cases treated with and without roentgen radiation during the period April 1, 1919, to April 1, 1922. One group of cases includes 31 patients in whom preoperative irradiation was employed and most of whom also received postoperative irradiation. The second group consisted of 36 cases receiving only postoperative irradiation. The third group contained, for comparison with the other two, 25 cases treated surgically without any irradiation.

Although the series includes a relatively small number of cases, the present study has convinced the authors that preoperative and postoperative irradiation are of value as an adjunct to surgery in the treatment of carcinoma of the breast. The best results were obtained when both preoperative and postoperative irradiation were employed. The end results will be largely determined by the plan of roentgen therapy followed and the dosage employed.

Clinical experience strongly favors the use of radiation prior to operation to convert, temporarily at least, a growing tumor into a regressive one. Preoperative irradiation is preferably given at two or three day intervals. As a rule four areas are exposed, two over the breast, one over the axilla and one over the supraclavicular region. The axilla is irradiated whether or not axillary nodes are palpable. The dose employed was delivered by 140 kv., 4 ma., 10 in. spark gap, through 4 mm. Al, target skin distance 10 to 15 in., for 7 to 15 min., depending upon the portal. This dose is usually followed by a first degree erythema in one to two weeks, and slight pigmentation in three to five weeks. The treatments therefore extend over a period of about ten days. The

best results appear to be obtained if an interval of at least three weeks is allowed to elapse between irradiation and operation.

Even with the best surgical technique dislodged tumor cells may be left in the operative field or may have escaped removal. This is the reason for using postoperative roentgen treatment. Such irradiations are usually given twice a week, the same area being exposed as in the preoperative cycle. Only a superficial dose is necessary over the anterior chest wall (the breast having been removed), whereas for the axilla and the supraclavicular regions a relatively greater depth dose seems indicated. Treatments are begun two weeks to the month after operation, when the wound has entirely healed and the patient fully convalesced. About five weeks should be allowed between the last preoperative exposure and the first postoperative treatment. This dose may be repeated once or twice, the cycles being separated by intervals of two or three months. At present it seems highly desirable to follow such a plan of repeated fractional dosage rather than to rely upon a single massive dose given postoperatively.

LAPENNA, M. Treatment of mediastinal tumors. *Arch. di radiol.*, Mar.–Apr., 1925, i, 247–257.

The patient was a woman of thirty with a lymphosarcoma of the mediastinum. Roentgen treatment brought about a slow but noticeable decrease in the size of the large mediastinal tumor and kept it in a relatively latent condition with decrease and even disappearance of the subjective symptoms of compression, disappearance of the fever and moderate decrease in the leucocytosis for a long time. But after an interval of sixteen months during which the patient was in good health and during which the tumor remained at the reduced size brought about by the first series of irradiations, the symptoms of compression returned in an aggravated form and increased until they brought about the death of the patient. In this last stage radiotherapy had no effect.

From a study of the case the author concludes that radiotherapy should always be tried in tumors of the mediastinum as early as possible; that sensitiveness to roentgen rays is greater in lymphogranuloma (mediastinal Hodgkin's disease) and that it responds most rapidly and effectively in the first stage; results, although less immediate and of briefer duration may also be obtained in lymphosarcoma in the beginning stage; that irradiation in lymphosarcoma should be given with large doses and should be repeated every time there are renewed signs of proliferation. The rays have no effect in the final stage in which the tumor has infiltrated surrounding organs, trachea, bronchi, etc., and has penetrated the deeper tissue. In the above case autopsy showed that the tumor had perforated the posterior wall of the trachea and projected into its lumen at the bifurcation, causing partial stenosis.

MUNDELL, JOS. J. Four years' experience with radium in the treatment of gynecologic conditions. *Am. J. Obst. & Gynec.*, July, 1925, x, 70–82.

The very early case of cancer of the cervix belongs to the domain of surgery, but such a case is a rarity. The proper handling of so-called borderline cases is still in dispute. Radium is a palliative agent of distinct value in the inoperable cases under which category fall the vast majority of cervical cancers seen in practice. In certain selected cases of uterine fibroids radium produces satisfactory symptomatic cure. In the cases of excessive menstrual flow at or near menopause in which no gross pathology is demonstrable radium is a specific.

NEW, GORDON B., AND FIGI, FRED. Treatment of fibromas of the nasopharynx; report of 32 cases. *Ann. Otol., Rhinol. & Laryngol.*, March, 1925, xxxiv, 191–196.

Experience has shown that fibromas of the nasopharynx belong to that group of tumors best suited to radium and roentgen-ray treatment; and radium is considered the treatment of choice. From 1910 to 1923, 32 cases of fibroma of the nasopharynx were observed at the Mayo Clinic. This includes only the hard fibromas. The average age of the patients was 18.5 years; 90.6 per cent were less than twenty-five years of age at the time of examination. The activity of the tumor seemed to be directly related to the age of the patient. Such tumors are more common in the male, only 4 of the cases in the present series being females.

Fibromas of the nasopharynx are microscopically benign and clinically malignant. The surgical treatment is usually attended with frequent recurrences and a high mortality. The severe hemorrhage accompanying such operations makes them hazardous. Of 8 patients observed before radium treatment was instituted, 5 were operated on by the avulsion method, and 2 died. The other 3 patients could not be traced. Three patients were examined only and not treated.

From 1915, 24 patients were examined and 23 were treated with radium. The treatment was applied by three methods. In early cases a T-shaped lead applicator with a 50 mg. tube of radium in a trough of the T was

held in various positions against the tumor in the nasopharynx. The original dose was usually a 50 mg. tube for ten to fifteen hours. Severe reactions in adjacent structures occur, which necessitate protecting the posterior surface of the palate with a 2 mm. lead retractor covered by a finger cot. In the second group of cases, steel points containing emanation or radium were inserted directly into the tumor. Depending on the size of the tumor, three or four points were usually inserted, about the same amount of radium being used as in the initial dose. In the third group of cases emanation seeds averaging 0.5 to 1.0 mc. were planted directly into the tumor, the number depending on the size of the tumor. Such treatments are repeated in from six weeks to two or three months, depending on the reaction and the result. The number of applications required in the cases now cleared up varied from two to nine, averaging between five and six. The average length of time before the condition cleared was 14.2 months. Of the 23 cases treated with radium, 15 are reported as cured, 4 as under treatment and the remaining 4 improved during treatment but could not be traced.

PILGER, W. Deep *x*-ray therapy. *J. Cancer, Dublin*, January, 1924, i, 9–21.

A preliminary report is given of deep roentgen therapy which has been carried out in the City of Dublin Skin and Cancer Hospital. The case reports given are on selected patients who have done well under the treatment. The methods pursued are based on the principles of the Erlangen school, using Symmetrie apparatus with gas and Coolidge tubes. As far as possible, the full dose required was administered in one day, the time in malignant cases extending up to six or seven hours. In general, the patients sustained this treatment with much less discomfort than an operation, and even in inoperable and advanced cases the patient is given a chance of being considerably improved or even cured without doing much harm. In the cases reported, none of them is more than six to nine months after treatment so that cure in the absolute sense of the word cannot be maintained.

Most of the epitheliomata and almost all cancers of the lip react well to the treatment; and the cosmetic result is excellent. Where glands have developed in conjunction with a recurrence in a scar the results are less satisfactory.

Cases of cancer of the uterus, of the intestinal tract, and of the breast are briefly described. The experience in cancer of the tongue shows that the results are not so good as in cancers of other parts of the body. If operation is not possible here, treatment is advised by diathermy combined with roentgen rays.

Tuberculosis of the bladder, of the cervical glands and lupus vulgaris were each treated with roentgen rays, with apparently satisfactory results.

PINCHERLE, PINO. Roentgen findings and roentgen therapy in pertussis. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, March, 1925, xxxiii, 211–214.

In uncomplicated cases of whooping cough the roentgenographic findings are as follows: The lung apex is normal, and there is pronounced accentuation of the hilus markings. Closer examination of this markedly branched shadow reveals numerous minute and medium sized annular shapes with very thick but uniform external contours. These structures are most numerous in the vicinity of the hilus but are visible also in small numbers farther away. The upper lobes always show many of these shapes. These are apparently small and minute bronchial lumina hypertrophied as the result of long repeated attacks of coughing. The number and appearance of these structures depends of course upon the duration and severity of the disease. The parenchyma often shows shadows of polycyclic contour comparable to bronchiectatic enlargements due apparently to rupture of the parenchyma and confluence of several dilated ampulla-like sacs.

In the complicated cases the above roentgen picture has superimposed upon it shadows caused by focal condensations of the lung tissue. The latter are of course usually bronchopneumonic infiltrations.

The roentgen treatment of pertussis has yielded very striking results. To date a total of 54 cases have shown greater or less improvement and only 3 remained unimproved because of intercurrent conditions. Naturally, none of the cases received treatment until the symptoms were more or less advanced. The roentgen treatment on the first day consisted of 3 H, portal 10 cm. diameter, filter 3 mm. Al, 28 to 32 cm. focal skin distance, 27 cm. spark, applied over the upper thorax. The second irradiation was given two days later, 3 H filtered through 3 mm. Al, over the upper portion of the back. Smaller children receive only 2 H. Most of the attacks began to disappear on the following day. A third irradiation was given four days after the last. The last dose was repeated if the patient showed improvement; if not, the dose was applied over the sternum. A fourth irradiation is rarely indicated. One case is described in detail.

RUMPF. Deep *x*-ray therapy in gynaecology. *J. Cancer, Dublin*, January, 1924, i, 43–47.

The two most important forms of deep roentgen therapy in gynecology are irradiation of the ovaries and irradiation of cancer. It is a matter of first importance that treatment shall be in the hands of trained specialists who have adequate apparatus and technique at their command.

Irradiation of the ovaries, if carried out carefully, is much to be preferred to an operation, and there is no longer any doubt about its superiority. The treatment of myomas is also simple since it is merely a matter of sterilizing the ovaries by roentgen rays. In the treatment of cancer the technique of irradiation differs according to the situation and peculiarity of the case. In general, it is necessary to carry out the treatment in two parts with an interval of seven to eight weeks. One problem for research is the elimination of the uncertainties in measuring dosage, and not until then will deep therapy be enabled to proceed to its logical ends.

VERSARI, ATTILIO. The treatment of lichen ruber planus by irradiation of the spinal cord. *Arch. di radiol.*, Jan.–Feb., 1925, i, 59–66.

Versari reviews the work of Pautrier and Hufschmitt in treating lichen ruber planus by irradiation of the spinal cord and describes two cases of his own in which the treatment was successful. His technique was as follows: The patient was laid on his face and the spinal column divided into eight fields, four on each side. The irradiation was given from the sides, the normal ray of the tube being inclined at an angle of about 45° to the spinal column in such a way as to cut the lamina of the vertebrae. Anticathode-skin distance 30 cm., filter 5 mm. aluminum, spark gap 30 cm., 2 ma. Each field was given a dose of 4 H, a dose larger than that given by the other authors, but he counted on part of it being absorbed by the lamina of the vertebrae. The rays were directed in such a way as to cross on the spinal cord.

Pautrier used irradiation for lichen ruber planus because he considered it, in part at least, a nervous affection, and Hufschmitt used it because, from the distribution of certain forms of lichen and from changes in the spinal fluid, he believes it to be an inflammatory process of the meninges of the spinal cord and roots. Versari believes however that the sympathetic is involved in its causation and as an argument in favor of this theory cites the fact that Pautrier had failures in some cases at first when he used the method of vertical irradiation and later had success when he used lateral irradiation, as with the latter method the rays strike the sympathetic ganglia along the spinal column. With frontal irradiation the irradiation of the sympathetic chain of glands is incomplete or insufficient and therefore treatment is a failure.

VOLTZ, FRIEDRICH. The exclusive treatment of collum carcinoma by radiation. *Klin. Wchnschr.*, July 16, 1925, iv, 1396–1401.

From 1912 to 1918 the Frauenklinik of Munich had a total of 755 cases of carcinoma of the neck of the uterus,—67 hopeless cases did not receive treatment and all the rest were treated with radioactive substances. Of those treated, 103 cases, 13.2 per cent, showed absolute cure as judged by the five-year survival period. A further group of 272 such cases seen in 1918 and 1919 showed 14.3 per cent cured after five years. These observations and similar ones reported from other clinics are definite proof that exclusive radiation therapy of gynecological carcinomas especially collum carcinoma, has not been a failure, especially when compared with results of surgical treatment.

The average absolute percentage cure after radiation treatment, without regard to the kind or method of treatment is figured at 16.9 per cent; the average relative percentage of cure obtained by radiation therapy in operable cases regardless of kind or method of treatment is 41.9 per cent. The average absolute percentage of cure by operation irrespective of the operator, is given as 26.9 per cent; and the average relative percentage cure by operation is 39.0 per cent. This comparison speaks in favor of operation, but one must keep in mind that the cases subjected to radiation treatment represent a more or less unfavorable residue after the surgeon has taken his pick of cases suitable for operation. This is brought out by the following figures: The average percentage operability of the cases entering clinics offering radiation treatment was 19.3; and the average absolute percentage healing from radiation treatment is 16.9. The average percentage operability of cases entering surgical clinics is 64; and the average absolute percentage cure of operation is 26.0.

A mere inspection shows at once that certain clinics report much better results than others for radiation therapy of carcinoma. The whole problem of efficient radiation therapy depends upon three important points: (1) application of adequate amounts of radioactive substances; (2) efficient apparatus for produc-

tion of roentgen rays, and (3) skillful and proven technique of irradiation. If these could be maintained in all clinics offering radiation therapy it is obvious that the results would not only be more uniform but would undoubtedly be improved. Additional factors tending to improve radiation therapy of carcinoma of the uterus are, irradiation of the hypophysis, improved radiation methods and elimination of roentgen sickness.

WINTZ, H. The preliminary and after treatment in *x*-ray therapy. *J. Cancer, Dublin*, January, 1924, i, 22–42.

Serious deep roentgen therapy cannot be confined simply to the application of the required dose of rays. All of the various factors necessary for avoiding injuries, on the one hand, and strengthening the body of the patient, on the other hand, must be kept in mind. Consequently, it is the duty of the roentgenologist to discuss the preliminary treatment with the internist working with him, and also to give his patients the necessary instructions. The object of the preliminary treatment is to render the conditions of the roentgen therapy as favorable as possible. This involves the psychological aspects, as well as the purely physiological. A thorough examination of the general health of the patient is essential and a careful roentgenographic examination must also be made before treatment. It is an invariable procedure in approved roentgen practice that the patient must undergo the treatment either fasting or after having partaken of a very light meal. If there are severe intestinal troubles it is preferable to wait several days rather than subject the patient to the radiations in such a condition. Both the preliminary treatment and the after-treatment depend naturally upon the nature of the case.

For example, after irradiation of a carcinoma, four principal conditions must be fulfilled: (1) rectification of the injuries caused by the radiations; (2) elimination of products from disintegrating tumors and neutralization of harmful products of metabolism of the normal cells; (3) the assistance of the body to continuing resistance against carcinoma, and (4) thorough restoration of healthy tissues in place of the original carcinoma. Far reaching as the alteration of the blood appears, experience shows that its original condition is restored in about six weeks after irradiation. A satisfactory result in the treatment of carcinoma is not dependent upon the properly carried out application of roentgen rays alone; very often the conduct of the after-treatment decides the result.

MISCELLANEOUS

BARCLAY, A. E. The history and future of British radiology. *Brit. J. Radiol.*, January, 1925, xxi, 3–20.

The growth of the various British societies and journals interested in electrotherapy, roentgenology and radiology is traced from their beginnings about twenty-seven years ago. The facts set forth should be interesting to the student of the history of radiology. Physics, on the one side, and medicine on the other, have become so widely separated that very few medical men have been able to keep pace with the advances in physics; and the medical problems are quite out of the line of the physicist. The true functions of the British Röntgen Society is regarded as lying on the borderland and in the practical applications, a sphere in which the instrument maker takes a large part, for it is on his adaptation of the progress of science to practical purposes that the progress in medical radiology depends.

BARLOW, GUY, AND KEENE, H. B. Experimental methods for testing leakage of emanation from radium tubes and applicators. *Brit. J. Radiol.*, January, 1925, xxi, 29–36.

Two general methods are described for the detection of leakage of emanation from radium tubes and applicators. In one it is necessary for the specimens to be brought to the laboratory for testing, and in the other the specimens do not leave the hospital, although the evidence for leakage may be examined in the laboratory at leisure.

The first method is called the capsule method. The radium tubes and applicators are brought to the laboratory and each is placed on a wire rest in a shallow square capsule of metal or glass which is closed with a greased glass lid. After a suitable exposure the specimen and wire rest are removed, and the capsule and lid are placed side by side without delay in the ionization chamber of an alpha ray electroscope. If leakage of emanation has occurred a typical decay curve of the active deposit will be observed.

The location of a leak in a capsule is a matter of more or less difficulty. The method tried which proved successful was to prepare a sealed capsule with window of sheet rubber. Through this window one end of the leaky capsule was inserted. The interior of the capsule was tested for active deposit after an exposure of one-half hour. The experiment was repeated with the other half of the tube inserted in the capsule and it was found that the leakage was associated with one half only.

Further tests made by inserting successively shorter lengths of the tube within the capsule showed that the leak occurred over an extended region near the middle of the tube which carried the deeply cut identification number. It is desirable that the loss of emanation from a leaking specimen should be expressed in some definite units, as curies per second.

The other method is to secure the occlusion of the leaking emanation in a thin film of some suitable material. Sheet rubber may serve the purpose but it was rejected in favor of vegetable charcoal, which was found to retain its occluded emanation for much longer periods of time even when freely exposed to the surrounding atmosphere. Cocoanut charcoal as prepared for high vacuum work but finely ground is very suitable. It may be used as a loose powder and after absorbing the emanation may be sprinkled out in a small tray and placed in the alpha ray electroscope. It was found more convenient to prepare it in the form of a thin coherent layer by mixing with rubber solution. Each radium specimen to be tested is inserted into a specially prepared stoppered bottle containing a mat of the charcoal-rubber absorbent and left over night. Next morning after an exposure of ten hours the specimens are removed, the stoppers replaced and the bottle returned to the laboratory for testing. If the mat is charged with emanation its activity will diminish very slowly with time, and consequently an appreciable time interval may be allowed to elapse before measurements are made. It is characteristic of a charged mat that if left in the electroscope a small increase in the apparent activity is always evident, due to the accumulation of emanation leaking slowly from the charcoal. This storage method of testing avoids not only the risk of loss of the specimens by their removal from the hospital, but also the objectionable practice of bringing leaking radium preparations into the physical laboratory.

Beatson, George Thomas. Case of osseous metastasis from primary carcinoma of the right mamma. *Brit. J. Surg.*, January, 1925, xii, 473–486.

The statement is made rather emphatically by Handley that in mammary carcinoma secondary bone deposits occur only in bones which lie partially or wholly in the area liable to subcutaneous nodules, that is, that the bone metastases are due to lymphatic dissemination and not to blood infection. A case is reported in a woman, aged fifty-five, which was examined at autopsy. A close study revealed that carcinoma of the right mamma was followed by a lymph spread to skin, glands, pleura, clavicle, skull and vertebrae. In addition there was a blood spread to all the long bones of all the limbs and to the liver, lungs and kidneys. The case described is therefore partly lymphatic- and partly blood-spread.

Roentgenograms showed that the cancerous foci were not more frequent in the tendinous or the fascial insertions. This point is well illustrated in the phalanges of the hand where the tendons are attached at the base while the foci were more numerous at the apices. Large nodules and masses of tumor tissue were also demonstrated in the radii, ulnae and fibulae, chiefly in the marrow cavity.

Bonanno, Matteo. Rapidity of sedimentation of erythrocytes in roentgenotherapy. *Radiol. med.*, September, 1925, xii, 638–647.

Bonanno reviews the different theories which have been advanced to explain the varying rapidity of sedimentation of the erythrocytes under different conditions. It has been found that erythrocytes, when subjected to an electrical current, collect at the positive pole, showing that they have a negative electrical charge. The erythrocytes of a pregnant woman approach the anode less rapidly than those of a normal man, showing that they have a greater electrical charge. There seems to be some substance in the plasma, especially in the fibrinogen, which has a positive electrical charge and which neutralizes the negative charge of the erythrocytes. Linzenmeier found that solutions of fibrinogen greatly decrease the negative electrical charge of the erythrocytes, while the withdrawal of fibrinogen from the blood by coagulation increases it. An increase of fibrinogen in the blood therefore would increase the rapidity of sedimentation of the erythrocytes.

It is generally agreed that roentgen irradiation increases the coagulability of the blood and it should therefore increase the rapidity of sedimentation of erythrocytes. The author examined 37 cases which had been irradiated with a view to determining the effect of the irradiation on sedimentation. The cases included ones of tumor of the hypophysis, metastases of cancer of the uterus and breast, leucemia, syphilitic splenomegaly, metastasis of renal tumor, pernicious anemia, sarcoma of the mediastinum, retroperitoneal tumor, fibroma of the uterus, depilation of the face, pruritus of the vulva, tuberculous lymphoma, and sciatica. Tables are given showing the rate of sedimentation in the different cases. The determinations were made before irradiation, immediately afterward, one hour and two hours afterward and in some cases during the whole period of the treatment. He concludes

that while in many cases there is increased sedimentation during the irradiation it occurs generally in cases where there is increased rapidity anyway from causes inherent in the disease itself, and that the increased rapidity only lasts for a few hours. It takes place more readily when very vascular regions are irradiated, especially the abdomen.

CLARK, L. H. The measurement of *x*-ray intensity by ionisation methods. *Brit. J. Radiol.*, January, 1925, xxi, 21–28.

It was decided to measure the ionization occurring when a beam of roentgen rays of constant intensity and quality traverses an air gap between two parallel plate electrodes, the distance between which can be varied. Making allowance for the change in capacity of the system with different distances between plates, any variations in the ionization readings must be due to the quantity of air ionized indirectly by radiations scattered from the main beam. By performing the experiment for a soft and for a hard beam of rays any observed difference will denote a change in the scattering effect of the air with the wave length of the main roentgen-ray beam. The measurements were made with the electrodes of the electroscope separated from 1.0 to 0.2 cm. For each setting, a series of simultaneous readings was obtained on the electroscopes for low output and moderate output. By plotting the readings, a series of curves was obtained from which were read the ionization currents for the different air gaps. When the appropriate corrections for capacity and natural leak are made the readings for soft radiation do not vary by more than 5 per cent. The figures obtained for hard radiation show a variation of 7 per cent. One may therefore conclude that the ionization produced at distances greater than one millimeter from the main path of the two roentgen-ray beams used is negligible under the given experimental conditions. With an air gap three times the width of the roentgen-ray beam the readings of the electroscope for moderate outputs are independent of any scattering effect produced by a column of air approximately sixteen times the width of the gap. With these figures in mind it is possible to construct an air gap ionization chamber in which the effect of radiation scattered from the air is insignificant.

FERRI, UMBERTO. A case of congenital fragility of bones. *Pediatria*, Jan. 1, 1925, xxxiii, 20–30.

A child four days of age was brought to the clinic with a fracture of the left humerus, certainly intrauterine, and one of the left femur which had probably occurred during labor. Within a short time thereafter it suffered five other fractures. The child was in good general condition and Wassermann examination excluded syphilis of the parents. The spleen was slightly enlarged and there was a considerable degree of craniotabes; there was no curvature of the long bones and no enlargement of the epiphyses. An examination of the calcium content of the cerebrospinal fluid showed that the total amount of calcium was ionic calcium, that is, that there was no calcium in organic combination. Four roentgenograms are given showing the appearance of the bones. There was no retardation of ossification, no change in the epiphyseal line and articular cartilages and no inspissation of the periosteum. The thinness of the cortex of the diaphyses of the long bones showed slight periosteal development of the diaphyses. The great permeability to roentgen rays showed a general deficiency of calcification. The trabeculae of the bones were not visible, evidently due to their slight calcification. There were none of the typical clinical or roentgenological signs of either rickets or syphilis, and infantile osteomalacia was excluded by the absence of general decalcification as shown by longitudinal striae. This was clearly a case of formative anomaly of the bones, corresponding in all points to the osteogenesis imperfecta of Vrolik. There were also slight vascular changes, blue sclera, slight hypertrophy of the spleen and abnormal leucocyte count, which are abnormalities of development that frequently accompany fragility of the bones.

The author concludes after a discussion of the symptoms given by various authors that osteogenesis imperfecta and osteopsathyrosis are the same formative anomaly of the osseous system, differing only in the period at which they develop and the degree of intensity.

He treated this case with ultraviolet rays giving 22 applications with a quartz lamp, in all seven hours of exposure to the rays, and found after this treatment that the relation of ionic calcium to total calcium in the cerebrospinal fluid had returned to normal and the white corpuscles had increased from 9,000 to 14,000, the increase being mostly in the neutrophils which had increased from 15 per cent to 32 per cent. The craniotabes was greatly reduced, the fusion of the frontal bones was completed and after this time the child did not have any fractures. There had evidently been an increase in the defensive power of the organism as manifested by the increase in leucocytes and an improvement in calcium metabolism.

FRIEDRICH, W., AND BENDER, M. New phenomena of secondary radiation and their significance for radiation therapy. *Strahlentherapie*, 1925, xix, 731–740.

All our tables of dosage showing the weakening or extinction coefficient of the primary radiation are based upon the assumption that primary and secondary radiations are of the same quality. The requirement of Dessauer that for correct dosage every tissue element of an irradiated organ shall receive rays of the same quality could not be fulfilled if, perchance, there occurred an alteration in wave length within the body. This last possibility seems to have been confirmed by the observations of Compton, although Clark and Duane oppose it. A series of experiments were made in which it is shown that water (regarded as the analogue of the biological object) does emit secondary roentgen rays of a complex nature when exposed to the influence of radiation of the platinum K_{alpha}-doublet and of wave length 0.19×10^{-8}cm. A comparison of the data for sodium with those for water disclosed no significant qualitative differences between these two materials as secondary radiators. However, the dependence of this new phenomenon upon the material of the secondary radiator should be of interest because in the biological object there are present substances of higher atomic number than the components of water.

The results show that the customary assumption of equality in wave length of primary and scattered radiation is no longer tenable. The question therefore arises: What significance have these new observations upon the practice of radiation therapy? Although the intensity of the scattered radiation of the second order is not very considerable and the change in hardness of the residual radiation is not very significant, still the matter is a subject that should be fully investigated. Also the effects produced in the intensely filtered non-uniform, harder radiation (of present-day deep therapy) such as that of the platinum lines employed in the present investigation because of their homogeniety, are probably from the nature of the phenomenon a rather common occurrence. These matters are now being investigated.

GARDNER, BOYD S. Safeguarding the patient and *x*-ray technician from infection in radiodontia. *Radiology*, August, 1925, v, 169.

Attention of physicians and dentists is directed to the possibility of infecting one patient from another in the process of exposing dental films. Assuming that the films coming from the manufacturer are fairly clean, the following technique has been used at the Mayo Clinic to avoid dangers of infection. The operator uses rubber gloves and does not change for each patient unless the condition of the mouth is questionable. However, the gloved hands are washed liberally with soap and water followed by alcohol before each case. A sterile towel receives all the films taken from one mouth and it is delivered to the dark room, the dark room operator taking precautions to safeguard himself. Between patients, everything that is touched by the operator's hands is wiped with 40 per cent alcohol and allowed to dry.

GLASSER, OTTO. The production of highly concentrated radium emanation preparations and their application in radiation therapy. *Strahlentherapie*, 1925, xix, 712–730.

Radon is the name assigned to radium emanation by international agreement, and the early general adoption of this term is desirable. Radon preparations can be applied for therapeutic purposes with exactly the same effect and in the same manner as radium salts. Radon, moreover, possesses several desirable features over radium; namely, it is not costly and therefore loss or damage is a minor consideration. (2) It furnishes the greatest concentration of radiating substance in a minimum volume; for instance, the gamma ray equivalent of 1 gm. of radium element corresponds, under normal conditions, to a radon volume of but 0.63 c.mm. (3) Radon being a gas is uniformly distributed throughout its volume and thus assures uniform distribution in all forms and sizes of applicators. (4) It is possible to prepare filamentous capillaries containing radon, thus improving the technique in the irradiation of tumor nests and extensions. (5) Radon may be applied in all the known forms of therapy; namely, alpha radiation, emanation water, etc. As against these advantages possible disadvantages are the inconvenient method of obtaining the radon and concentrating it, as well as possibly the inconvenience in calculation of dosage.

The properties of radon are briefly outlined and a detailed description is given of the two methods of obtaining the emanation. These are the methods of Rutherford and of Duane. Precautions to be observed in the handling of the material boil down to three essential points: (1) protection of personnel working in the vicinity of the radon room; (2) protection of the various ionization instruments against contamination with radon, and (3) protection of radium against theft.

In calculation of the strength of radon preparations it is of course essential to take

into account the decomposition of the preparation. Such calculations are made with the aid of the well-known exponential law of decomposition; and for practical purposes the decomposition for each twelve-hour period can be read off from tables furnished with the standardization of the preparation. Moreover, the amount of disintegration for the interval during which the radon is being applied must be determined so that the full dose in millicurie-hours can be secured. For this purpose the graphic method described by Failla is to be recommended. This easily permits exact dosage.

HERZOG, FRITZ. The effect of roentgen rays on blood regeneration. *Strablentberapie*, 1925, xix, 759–771.

The favorable results obtained with roentgen rays in pernicious anemia by Bucky and Guggenheimer, using small stimulative doses, suggested the possibility of improving the activity of the erythropoietic system by such radiation. Experiments to test this notion were performed upon guinea pigs. Mild doses of radiation were administered by Symmetrie apparatus, with Coolidge tube, 3 ma., 125 peak kv., distance 23 cm. The results show that direct irradiation of the bones, even in small doses, causes an injury to the blood forming elements. A brief general irradiation likewise causes an interruption in blood formation at first, but this is followed by an accelerated output which soon compensates for the original loss and leaves a net result of increased output of blood elements. In one experiment where unfiltered radiation was applied over the whole animal, the effects observed were similar to those seen after parenteral administration of protein, resulting in an acceleration of production.

Keeping in mind the fact that these observations cannot be directly transferred to human therapy, it nevertheless indicates that general irradiation may be a hopeful weapon in the treatment of torpid human anemias. Clearly a direct irradiation inhibits erythropoiesis but brief general irradiation may, under certain circumstances, favorably affect regeneration following blood loss. Apparently the stimulating effect upon the bone marrow is an indirect one.

HESS, ALFRED F., AND WEINSTOCK, MILDRED. Antirachitic properties imparted to inert fluids by ultraviolet irradiation. *J. Am. M. Ass.*, Dec. 6, 1924, lxxxiii, 1845–1846.

Experiments have pretty well established that irradiation with ultraviolet light of oils such as linseed oil or cottonseed oil imparts to the latter a curative effect on human and animal rickets. Liquid petrolatum, when irradiated, has remained inert.

Report is made of attempts to induce antirachitic properties by means of fluids containing radium. Water to which radium bromide had been added in very small amounts was fed daily without any antirachitic effect. This was true likewise with regard to linseed oil to which minimal amounts of radium had been added. Failure also resulted with subcutaneous injections of radium water.

LESSHEIM, KURT. A side effect of radiothorium hitherto not observed. *Klin. Wchnschr.*, Aug. 20, 1925, iv, 1645.

General experience has shown that the range of dosage of radiothorium for the treatment of leucemias appears to lie between 20 and 100 e.s.u.

The peculiar side effect was observed in a patient suffering from typical myeloid leucemia. He received 200 e.s.u. of radiothorium in the right cubital vein, and a general improvement in the blood condition followed. Four months after the injection the patient presented a vigorous healthy appearance except for the following condition of the right arm. Four weeks after the injection the patient observed a slight itching at the site of injection. Two months later the right elbow was much reddened, with a bluish cast. The skin was dry and non-elastic; elbow could be flexed fully but not stretched. A month later the color had grown deeper and the markings of the lymph channels were somewhat less pronounced. The whole picture was similar to that produced by a deep roentgen-ray irradiation. A photographic plate exposed for ten hours over the arm showed a partial blackening which was most intense at the site of injection and decreased farther down the forearm.

In the first place it is conceded that the dose of radiothorium was probably too great. It is supposed that the symptoms in the arm were caused by a thrombosis of the cubital vein at the site of injection, or else by a leakage of injection fluid around the vein.

HOLTHUSEN, H. The prerequisities for the inception of cell injury by roentgen rays. *Klin. Wchnschr.*, Feb. 26, 1925, iv, 392–395.

A sharp distinction must be made between the primary reaction due to the absorption of the rays and the secondary processes following. It is still a matter of controversy as to whether the primary process is a physical alteration of state of the tissue or whether it is a radiochemical effect following the absorption of

roentgen rays by radiosensitive molecules. In considering the later reactions it is to be noted that they proceed unlike the usual photochemical processes in a living system. Their course is apparently intimately bound up with the life processes of the irradiated organ or tissue; and they are likewise subject to the most diverse influences. At present the main point of differentiation is the fact that the primary insult is separated from the secondary effect by a time interval known as the latent period.

A series of experiments upon the spleens of guinea pigs and rabbits shows that when the blood circulation is stopped the appearance of the secondary reactions is delayed but the susceptibility of the cells to the radiation is affected only slightly. A decrease in sensitivity does occur as a result of elimination of the blood supply, apparently in proportion to the duration of the anoxybiosis. This, however, should be confirmed by a larger number of experiments. A decrease in sensitivity during anoxybiosis would appear plausible from what is known of the effect of variation in blood supply. The important thing is not so much the presence or absence of oxygen as the disturbance of metabolic reactions occurring in the growing cells as a result of oxygen-want. The resulting change in sensitiveness is but a gradual one and not to be compared with the effect of abolition of circulation upon the latent period of the roentgen injury process.

Levy, Leonard A., and West, Donald W. The photometry of *x*-ray fluorescent screens. *Brit. J. Radiol.*, July, 1925, xxi, 104–123.

The utility of fluorescent screens and their suitability for visual examinations depends upon four main factors: (1) the brightness of the screen when fluorescing; (2) the contrast between the bright and dark portions; (3) the sharpness of the image, and (4) the resolving power, that is to say, the power of the screen to differentiate between objects, the transparencies of which to the incident radiation differ by very small amounts. Only the brightness of the screen is susceptible of actual measurement expressible in numerical terms. A large number of experiments were made in which the different factors involved were varied. The results of the tests are plotted in a number of graphs so as to show the variation of the luminescence of the screen under various conditions. Three different photometer heads were used in the experiments and every photometric reading was independently made by two observers, whose readings were found to be in very good agreement.

The illumination exhibited by a fluorescent screen depends upon a large number of factors and varies considerably according to the fluorescent substance employed and the hardness or softness of the radiation. Cadmium tungstate screens are the most suitable for every purpose and are more responsive to the harder radiations than willemite. The latter substance gives brilliant results with unscreened rays but its luminosity falls off with increased hardness so as to be of little value practically. Barium platinocyanide screens are responsive to hard radiations but their illuminating power is not so high as the cadmium tungstate screens.

Measurements of the illumination of the screens show that, in general, more brilliant illumination is obtained with the gas tube than with a Coolidge tube; and more with a coil outfit than with a transformer outfit.

The practice of backing fluorescent screens with a sheet of aluminum is very undesirable. Even 1 mm. Al causes a reduction of the luminosity in the case of the cadmium tungstate screen of 12 per cent; with barium platinocyanide of 20 per cent, and with willemite 40 per cent. These figures refer to 99 kv. excitation only. The lead glass protective cover does not have any appreciable effect in absorbing the light in a cadmium tungstate screen but has a marked effect in the case of a willemite screen. Apparently the lead glass absorbs green light selectively to a certain extent.

It is difficult to postulate a standard of brightness for fluorescent screens unless the apparatus and conditions of measurement are accurately defined.

Loughborough, G. T. Acute *x*-ray burns. *Brit. J. Radiol.*, July, 1925, xxi, 135–140.

Roentgen burns are produced either through ignorance, careless technique, or insufficient protection. Everyone using roentgen rays should have special qualification. As regards technique, one common error is starting to demonstrate a case on the screen before the eyes have become accommodated. Another point is prolonged screening with too wide a diaphragm opening. This is quite useless and releases an added amount of scattered radiation. The use of a Coolidge tube with its stability of operation is a temptation to prolonged roentgenoscopy, especially where something interesting is to be seen. When a transformer is used for roentgenoscopic work an unduly large proportion of soft rays is given off. A small subsidiary coil should be used for screening wherever possible, the transformer being employed for making the exposures only. It is important to keep a careful record of all the negatives taken and screen examina-

tions made, so that if repeats have to be done an estimate of the amount of rays received by the patient can be made.

LÜDIN, MAX. Blood sugar increase in the rabbit following roentgen irradiation. *Strahlentherapie*, 1925, xix, 772–778.

Radiation was applied to the uncovered back of the rabbit, the tube being centered over the liver region, with the whole back included in the cone of rays. The radiation was delivered through a self-hardening Müller boiling tube, skin focal distance 30 cm., 2 ma., hardness 230 Sklero-Klingelfluss, time 2 hours. Blood sugars were determined by the Bang method. Animals irradiated fourteen hours after the last feeding and remaining unfed for ten hours further, showed a pronounced increase in the blood sugar value in the first fifteen minutes following irradiation. The blood sugar then decreased rapidly for several hours and was succeeded by slower decline, so that after twenty-two hours the value was about normal.

In animals that were starved, roentgen irradiation caused no blood sugar increase but if anything a distinct drop for four hours after treatment. These observations may be taken to mean that the hyperglycemia produced by roentgen rays in the first set of animals is analogous to the effect caused by stimulation of the sympathetic system; and the hypoglycemia produced by irradiation of starved animals may be regarded as the effect of stimulating the parasympathetics.

An experiment was tried in which the parasympathetic was paralyzed with atropin. Irradiation of the liver of a starved animal thus atropinized resulted in the same pronounced hyperglycemia such as was found in the normal animals. These observations seem to indicate that liver cells injured by roentgen rays produce different sympathetic and parasympathetic influences depending upon whether the animal is starved or not.

MARKÓ, D. A new tubular arrangement for protection against radiations. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, March, 1920, xxxiii, 208–210.

The arrangement suggested consists in coating the roentgen tube with a protective material. Lead rubber is elastic and sufficiently absorbent for roentgen rays, as well as electrically nonconducting, to answer this purpose. The ordinary heating of the roentgen tube is apparently not sufficient to affect the rubber coating. In case it is necessary to separate the rubber sheath from the tube owing to excessive temperatures, the sheath is fixed so as to leave a small air space between it and the roentgen tube. A window of suitable size is cut in the focal path of the target to provide an outlet for the useful radiation.

This arrangement possesses two technical advantages: (1) it furnishes complete protection against primary roentgen rays to the physician and his assistants; (2) by means of parallel double screens a tube effect is attained which greatly improves the contrast effect. These are of advantage in roentgenoscopy as well as in roentgenography.

MILANI, EUGENIO. Roentgenographic and histological changes in the skeleton after experimental irradiation of the thymus. *Arch. di radiol.*, Jan.–Feb., 1925, i, 1–6.

Rabbits one month and twelve days of age and dogs twenty, nineteen and seventeen days of age were given irradiations of the thymus to determine its effect on growth of the skeleton. Some of the rabbits were given very small doses, only one minute or one minute repeated twice (¼ ma., 25–32 cm. distance, 1 mm. aluminum or without filter), others were given fifteen minutes (Coolidge tube, 2 ma., without filter or 1 mm. aluminum) and still others ten minutes at a time at intervals of a week for several weeks. The ones given the very small doses did not show any changes in development, although histological examination showed characteristic changes in the lymphoid cells of the thymus, which however were temporary. No changes in Hassall's corpuscles. The rabbits irradiated once for fifteen minutes showed temporary disturbance of growth, the more pronounced the younger the animals were. But after about four weeks they began to gain and caught up in development with the controls. But ones irradiated for thirty, forty or sixty minutes remained permanently stunted in growth. When the control animals weighed over 4 kilograms they only weighed 700–750 gm., and at the end of six months did not weigh more than 800 gm. The subcutaneous fat was poorly developed, the animals dragged their hind legs, the skin lost its elasticity and the hair fell out in spots on the neck and flanks.

The changes in the development of the dogs were about the same, but the thymus functions in the dog only about two months, so that only animals irradiated very young were affected. Histological pictures of the bones are reproduced which show that the characteristic change is a great increase in the articular cartilage; the columns of cartilage cells appear more numerous and pass irregularly into the epiphyseal and diaphysial tissues.

The cortex seems to be very thin. The results are similar to those obtained by thymectomy of rabbits.

PENNETTI, G. Bilirubinemia from ultraviolet rays. *Arch. di radiol.*, Jan.–Feb., 1925, i, 51–59.

Little attention has been given to the possible injurious effects of ultraviolet rays which are the active agent in the treatment of various diseases by sunshine. The author experimented on dogs weighing from 5 to 8 kg., exposing them for various periods of time to the rays of a Bach mercury lamp. He used Ehrlich's and Sabatini's methods for determining the bilirubin content of the serum. He gives tables showing the direct immediate and retarded actions and the indirect immediate and retarded actions by the technique of Ehrlich and that of Sabatini. He found that with small and medium doses of ultraviolet rays there was increase of red cells and hemoglobin but no quantitative change in the amount of bilirubin in the serum. Very heavy doses of the rays (about 40 hours' exposure to a Bach lamp) caused decrease of erythrocytes and slight decrease of hemoglobin with increased bilirubin. These cases almost always gave the indirect immediate reaction with either Ehrlich's or Sabatini's reagent. The bilirubinemia was not very intense and was of brief duration when the rays were discontinued and may be due to exaggerated hemolysis. De Martini has shown that in cases of exaggerated hemolysis the bilirubin in the serum may remain normal if the other organs, the liver and kidneys especially, are capable of compensatory hyperfunction. But if this is not possible because of lesions of these organs or because they have passed the limits of their capacity for hyperfunction there is an increase of bilirubin in the blood.

PERONA, PIETRO, AND OMIZZOLO, LAUREANDO B. Contribution to a roentgenological study of the outline of the lungs. *Radiol. med.*, September, 1925, xii, 616–623.

The authors made a roentgenological study of the lungs in the normal cadaver with a view to determining whether the lung outline is really produced by the vessels alone or whether the bronchi also take a part in it. They give seven roentgenograms taken with a technique almost the same as that described by French authors, injecting the bronchial tree progressively with 10 per cent iodoleine, taking care to avoid the least movement of the cadaver. Some of the roentgenograms were taken in the anteroposterior and some in the posteroanterior direction. In this way, comparing roentgenograms of the injected bronchi with roentgenograms made before the injection the authors proved that certain lines in the pulmonary outline correspond exactly in size, topography and course to sections of the injected bronchi. It is easier to demonstrate this in the upper lobes than in the lower. Though they agree that the lung outline is predominantly due to the vessels and the great caution must be exercised in reaching conclusions in regard to it the authors agree with Cluzet and others that under some conditions the bronchi may be visible when there is no pathological change in them.

PHILLIPS, C. E. S. Constant voltage high tension generators. *Brit. J. Radiol.*, July, 1925, xxi, 91–103.

It cannot be yet claimed that the constant high tension apparatus is more effective than the best modern transformer or coil outfit. It has, however, the advantage of making the milliammeter reading approach nearer the truth; and also, it introduces a welcome simplification into the expression of the conditions under which rays are used.

Attention is recalled to the experiment of Lumière in 1881 in which it was shown that the photographic effect of a continuously applied light was markedly greater than that produced by the same light when rendered intermittent, care being taken that the total time of exposure was the same in both cases. This matter has a direct application in roentgenology and is well worth following up. There must undoubtedly be an appreciable difference between the outputs of constant voltage apparatus and of the transformer type. The constructional features of the generators manufactured by Gaiffe, by General Radiological and Surgical Company, and by Watson and Sons are given.

RAHM, HANS. Pulsating or constant high tension direct current in roentgen therapy practice. *Klin. Wchnschr.*, June 25, 1925, iv, 1261–1262.

The following advantages are being urged in favor of the uniform high voltage current for operating roentgen apparatus. The roentgen tube works more smoothly and is under less strain; the time for administering a skin unit dose is considerably reduced (51 per cent or more) because of the greater number of hard rays traversing the filter; the homogeneity of the radiation is improved and the voltage at the tube is better. In order to test some of these claims the author made a series of measurements on his neo-intensiv-apparat to which had been added a set of condensers

connected in parallel with the roentgen tube. A considerable deviation was found for the minimal wave length λ_0 at maximum voltage as measured spectrographically. It is recommended that a calibration curve for λ_0 be constructed after the apparatus is set up. Only such a calibration can be depended upon. For the sake of uniformity data on maximum tube voltage should be determined spectrographically. It would seem desirable to have the condensers of the variable type so that adjustment can be made to the most favorable capacity since many factors such as primary voltage, discharge time, resistance characteristics of the tube, etc., all play an important part in the operation of the apparatus. Only when all these factors are taken sufficiently into account does the constant direct current in roentgen practice constitute an improvement over the pulsating current. The glowing statements in favor of the constant voltage operation are not yet justified.

RAHM, HANS. Contribution to the problem of homogeneous radiation. *Klin. Wchnschr.*, Apr. 16, 1925, iv, 754–756.

A description is given of a water chamber for use in the irradiation of the extremities. The device consists of a rectangular aluminum box with glass windows. Two ends are furnished with openings through which the extremity is inserted. These openings are fitted with rubber sleeves so arranged that they can be bandaged to the extremity and made water tight. The chamber is then filled with water, previously warmed to body temperature, The radiation is administered through the glass windows.

RISSE, OTTO, AND POOS, FRITZ. Roentgen rays and internal secretion. *Klin. Wchnschr.*, Jan. 8, 1925, iv, 60–62.

It is a well-known fact that under certain conditions increasing dosage of roentgen rays is accompanied by progressive decrease in the blood sugar which, in very favorable cases passes below the limit which, according to recent theory, should lead to symptoms of hypoglycemia. Opposed to these results are some recent observations showing an increased adrenalin secretion as a result of roentgen irradiation. In an attempt to test this last assertion experiments were performed upon the rabbit iris according to Trendelenburg's method, which is capable of revealing variations of 0.05 to 0.1 thousandths of a milligram per minute per kilo. In 7 rabbits receiving a total of 10 irradiations, the results by this test were definitely the opposite. Apparently there was some antagonism which over-balanced the expected effect of the adrenalin. An investigation into this matter revealed that apparently insulin in the arterial blood was the antagonist responsible for the above effect. This of course also furnishes an explanation for the pronounced drop in blood sugar following irradiation.

RODGERS, R. CRAIG. The organization and equipment of *x*-ray rooms arranged for private radiologists. *Brit. J. Radiol.*, July, 1925, xxi, 124–134.

The primary requirement is a house sufficiently large to be well ventilated, in a central area accessible for patients, but remote from noisy traffic with the risk of jarring instruments and annoying patient and operator. The private roentgenologist must possess similar equipment to that required in a roentgen-ray department of a hospital, but of course on a very much smaller scale.

Detailed descriptions and plans are given of the organization and equipment under the following heads: fluoroscopy, roentgenography, diathermy, ionization, ultraviolet radiations, treatment, photography, office, viewing, workshop, lavatories, examination, service room for charwoman, plate store (loading room), roentgenologist's study, dressing rooms, coal and coke storage, central heating.

ROFFO, A. H. The effect of roentgen rays on heart tissue cultivated *in vitro*. *Strahlentherapie*, 1925, xix, 745–758.

Studies were made upon *in vitro* cultures of the heart tissue of chicken embryo. These experiments were carefully controlled in duplicate. In one series the radiation was applied to the tissue *in vitro* immediately upon transfer to blood plasma, and in the second series the radiation was applied after twelve hours of incubation when there was already apparent a zone of new growth. The amount of radiation applied in each of these experiments was greater than the erythema dose, the dosage being 100 to 200 kv., 5 ma., 20 to 60 cm., from 10 to 220 minutes. It will be noted that some of the values for the dosage exceed by far the limits found by Kroenig, Seitz and others as fatal for the mature muscle *in vivo*.

It was found that the artificially cultivated heart cells are resistant to both soft and hard rays. There was not observed in the cultures that developed any destructive action, nor was there apparent any appreciable retardation in growth. The reason for this behavior is not apparent. The tissue cells seemed to retain their ability to grow and their normal embryonic appearance, yet they failed to respond to the rather extreme treatment imposed.

Schiassi, F., Comelli, U., and Possati, A. Clinical and radiological study of constitutional anomalies of the digestive tract. *Radiol. med.*, September, 1925, xii, 593–613.

I. *Common Mesentery, by Dr. Francesco Schiassi.* Before the discovery by Haudek and Åkerlund of a definite roentgenological sign of gastric and duodenal ulcer many such cases were regarded as ones of functional neurosis, and the author believes that almost all, if not all, so-called functional disorders of the digestive tract have been or will be proved by roentgen examination to have an anatomical foundation. He describes a case of that anomaly of position of the intestine which is called common mesentery. The whole mass of the small intestine lay on the right side and the cecum on the left, and the last loop of the small intestine emptied into the cecum after passing from right to left. This is due to an arrest of development at about the third month of intrauterine life. At about the sixth week the intestinal tract lies in the middle of the abdomen and is joined to the posterior wall of the abdomen by the primitive mesentery. Toldt's umbilical loop lies about the middle of it; its upper arm elongates and gives rise to the small intestine, while the cecum and ascending and transverse colons originate from the lower arm. There is a period at about the third month when almost all the small intestine lies to the right of the median line of the abdomen and all the large intestine to the left and these two segments are fixed to the posterior wall of the abdomen by the common mesentery. If rotation stops at this point it produces the condition described in Schiassi's case.

This patient had dyspeptic, vagotonic symptoms which she had had for many years, which the author thinks were due to the anomaly of development, as such an anomaly in any segment of the intestinal tract may give rise to vagotonic gastrointestinal disturbances.

II. *Free Duodenum, by U. Comelli.* Two roentgenograms are given of the case described, in which the duodenum, including the duodenojejunal flexure, although the latter could not be very clearly distinguished, lay to the right of the midline, with consequent inversion in the topographical arrangement of the loops of the jejunum. This is a lesser degree of the anomaly described by Schiassi, and is characterized by lack of fixation of the duodenum because of abnormal persistence of the embryonic mesentery. It also occurs at the third month of intrauterine life, as does Schiassi's anomaly. The clinical symptoms were indefinite and were attributed by the patient to a slight trauma suffered during his work, which of course was an entirely mistaken interpretation of the facts.

III. *Common Mesentery, by Alberto Possati.* The author gives diagrammatic illustrations of the course of embryonic development of the intestine and five roentgenograms of a case of common mesentery in a woman of twenty-three. The case was very similar to Schiassi's with the small intestine in the right half of the abdomen and all the colon on the left, and was due to the same embryonic arrest of development at the third month. The clinical symptoms were a feeling of weight and pain in the epigastrium, acid eructations, persistent dilatation of the pupils and marked Dagnini's sign, all signs of vagotonia which the author thinks were due to the constitutional anomaly associated with the anomaly in position of the intestine. He emphasizes the importance of examining the whole gastrointestinal tract in all cases of digestive disturbance.

Schreus, H. Th. The course of roentgen erythema, with histological studies. *Deutsche med. Wchnschr.*, Feb. 27, 1925, li, 358–359.

The observations of Miescher have been confirmed. The first erythema wave occurs ten to twenty days after irradiation; and the second, often the strongest, wave occurs between thirty and forty-five days. As is well known there is a certain level of dosage which produces a maximum erythema and further increase of dose produces no greater erythema, although sometimes a burn or dermatitis may result. Possibly the determination of the dose just necessary to produce a maximum reaction of the blood vessels may prove to be a harmless method of determining biologically the maximum tolerated dose of roentgen rays for a particular roentgen outfit and filtration. This dose would, of course, vary with the size of the field. With smallest fields and very hard rays, filtered through 0.5 mm. zinc, 40 cm. spark gap, Symmetrie apparatus, a dose of 900 R was found to produce this maximum reaction of the blood vessels.

Histological studies have also confirmed the beautiful results described by Miescher: amitotic nuclear divisions in the dermal tissues, especially the epithelium, sweat glands, and the endothelia of the blood vessels. It is particularly significant that amitoses occur also in the epithelium without its showing visible reddening. It is still a question whether there is any relationship between the nuclear divisions and the waves of erythema. The administration of about 900 R, relatively hard rays, unfiltered or through 0.5 mm. Al, when delivered through *very small portals* does not produce an erythema, and assuming that

the standardization of the instrument was correct, it is suggested that the absence of an erythema may be due to the fact that participation of adjacent tissues has been eliminated.

TANDOJA, P. Roentgenological findings and operative findings. *Arch. di radiol.*, Jan.–Feb., 1925, i, 7–10.

The author urges correlation of the roentgenological and operative findings in every case of operation for ulcer of the duodenum, in order to systematize the different roentgenological findings and relate them to the anatomical and functional changes in the bulb of the duodenum. The most successful attempt of this kind that has as yet been made is that of Åkerlund but in the 4 cases the author has studied he finds that only one corresponds to the type of Åkerlund. This is comprehensible in view of the different anatomical lesions in different cases and the different technique used in examinations. The author gives roentgenograms of his 4 cases with a summary of the clinical and roentgenological findings and suggests a technique for making the examinations.

The patient is given an enema to empty the intestines, told to drink the barium suspension slowly and laid on his left side. He should be rotated during the roentgenoscopy always from right to left, in order not to interrupt the current of barium chyme toward the pylorus and duodenum. During this movement of rotation the examiner looks for the most favorable position of the patient in which the antrum, the bulb and the second portion seems to be well dissociated and makes a mark on the skin of the back at the point where the rays should enter in making the series of roentgenograms. To get very clear images of the bulb, as it is generally in a condition of abnormal contraction and spasm, the author prefers rapid exposure in $\frac{1}{50}$ to $\frac{1}{10}$ second with hard tubes. A second examination is made after two hours when the terminal part of the stomach, the bulb and the second portion are better filled, which is necessary for the appreciation of any deformity of the bulb; the degree of emptying of the stomach may also be examined at this time. A third examination is made after six hours to determine the complete emptying of the stomach and the passage of the chyle through the ileum to the cecum.

The second day the colon is examined with the patient standing, particular attention being given to the appendix and the hepatic flexure. On this second day the series of roentgenograms of the pyloro-duodenal region is repeated and one made of the hepatic flexure of the colon. The repetition on the second day is particularly necessary in cases where pylorospasm has impeded the passage of the chyme into the duodenum. If the spasm persists on the second day the author uses atropin, papaverin and has the patient lie for a long time on his left side. In a few cases he has had to have the patient return after a few days of milk diet and use of antispasmodics.

On the third day the emptying of the colon and appendix are studied and the examination of the stomach repeated.

VAN EWEYK, C., GURWITSCH, MINNA, GOTTHEIL, CAROLA, AND GASIUNAS, I. Experimental studies on the effect of radium bromide upon metabolism. *Strahlentherapie*, 1925, xix, 789–795.

Radium in large doses produces an increase in the nitrogen metabolism leading to a decrease in blood lipoids but causing no apparent disturbance in the carbohydrate metabolism. This leads to a dehydration of the body but causes no great disturbance to kidney function as regards nitrogen and water excretion. The net result of the radium effect, therefore, is a general loss in weight. This emaciating effect of radium is caused, among other things, by parenchymal injury resulting in breakdown of body proteins, because resorption of food from the intestinal canal appears to go on in normal fashion. It is only when acute local injury occurs in the gastrointestinal canal that we have disturbance of nutrition, symptoms of hunger, and failure of normal intestinal absorption.

The above conclusions are based upon an experiment on a dog weighing 4.8 kilos which received one million Mache units radium bromide dissolved in physiological saline (208,333 Mache units per kilo). This corresponds to a dose of 14.5 million Mache units for a human weighing 70 kilos. The dog died fourteen days after the injection. Autopsy showed severe damage in the intestines, kidneys and bladder.

PUGNO VANONI, ENZO. Contribution to roentgenological technique. *Radiol. med.*, August, 1925, xii, 556–568.

1. *Measurement of high tensions.* After having mentioned the fact that to determine the quality of the radiation produced it is necessary to know the *maximum* value of the tension applied to the tube generator of the rays, the author rapidly reviews the methods employed at present for this purpose, pointing out the errors which are brought about by kilovoltmeters placed on the primary circuit, as well as the difficulty in applying exact

laboratory methods in roentgenological technique.

He then describes an electrostatic apparatus which makes it possible to measure continuously the maximum value of the tension applied to the tube, showing that this new instrument also gives information on the fluctuations of tension in installations with condensers, and that it makes it possible to measure exactly the tension needed in the tube of installations for diagnosis without making use of tension rectifiers. A prospectus included in the report shows that the information given by this apparatus coincides with that furnished by a spectrograph.

2. *Apparatus for roentgenology at a constant tension.* The utility of furnishing tubes with a constant current having been demonstrated, according to the author, for purposes of roentgenology, he reviews the different methods employed for this purpose up to the present time. As a triphase system is always made use of in industrial plants for the conversion of alternating currents into continuous currents he emphasizes the advantages offered in roentgenological technique by the adoption of triphase transformer-elevators, reporting some experiments which he has made recently with an apparatus constructed on the above principles. From experimental results (oscillograms of the tension obtained with the aid of a special instrument; studies of the emission of the tube), as well as from theoretical considerations the author shows that it is possible to obtain in this way very powerful apparatus which can furnish continuous differences of potential either with very high tension for therapy or with great intensity for diagnosis.

WADA, HIDEO. The effect of repeated radium bromide injections on the blood picture and the body weight also on the fixation and duration of radium in the organism. *Strablentberapie*, 1925, xix, 779–788.

Previous experiments with rabbits had shown that a single injection of 200 to 1000 Mache units of radium bromide per kilo of body weight had a stimulative action on the blood forming apparatus. Present experiments show that the above method of single dosage is better than a series of divided doses. Next in preference is the method of continued feeding with minute amounts of radium bromide.

Radium bromide, once it has reached the blood, was found to leave the body very slowly. After a single injection of 200 to 1000 Mache units per kilo considerable quantities of radium were still to be found in the bones and the bone marrow months later. Some experiments with dogs showed that feeding for several months with radium bromide left the bones and bone marrow practically free of radium, thus indicating that significant quantities of radium bromide are apparently not absorbed from the intestine.

Histologic examinations of the tissues of animals injected intravenously with radium bromide showed no changes in the liver, kidney, testis or ovary that could be considered parenchymal damage due to radium.

In radium bromide therapy the foregoing observations should be kept in mind. In intravenous injections the danger of cumulative effects is very great; on the other hand, per os administration of radium offers comparatively slight danger of a cumulative effect, except for a possible direct action on the mucosa of the gastrointestinal tract.

VEIEL, FRITZ. The treatment of roentgen ulcers with warm poultices. *Klin. Wchnschr.*, July 9, 1925, iv, 1356–1357.

Three cases of severe roentgen ulcers treated for a relatively short time, two to four months, were permanently relieved with good cosmetic results by use of the poultice described below.

The paste is freshly prepared each morning. Linseed meal is mixed with milk or water and cooked until a spoon stuck vertically into the paste remains standing. The paste is then inclosed in a double layer of gauze and is ready for application. It is preferable to have two such packs so that the reserve one may be kept warm on a hot water bottle or preferably a tin box containing a warm water bath. Thus, a warm poultice may be substituted as soon as the one in use has become cold.

WALTER, B. What is the time required to produce an erythema dose through protective gloves? *Fortschr. a. d. Geb. d. Röntgenstrahlen*, March, 1925, xxxiii, 231–236.

A calculation is made of the quantity of electricity put through a roentgen tube delivering radiation of hardness 7 W, skin focal distance 50 cm., to produce an erythema through gloves of different thicknesses. The erythema dose is 160 ma-hr. for gloves of 0.1 mm. lead equivalent; 1000 ma-hr. for 0.2 mm. lead equivalent; 4000 ma-hr. for 0.3 mm. lead equivalent, and 20,000 ma-hr. for 0.5 mm. lead equivalent. These values are of course maximum values since they apply to continuous irradiation for the production of the erythema dose.

It is suggested that the roentgenologist protect hands and face so far as possible with the equivalent of not less than 3 mm. lead.

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